

Sensitivity analysis and numerical simulation of the dynamics of cholera transmission with vaccination and pathogen mutation: Implications towards control in Kenya

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Abstract

This study applies sensitivity and a numerical simulation of a deterministic cholera transmission model to consider vaccination, pathogen changes, sanitation and environmental contamination. The basic reproduction number (R_0) was calculated through next-generation matrix method and a base value of $R_0 = 0.78398$ was found. All model parameters were also normalized to identify which ones have the highest effect on the transmission of cholera. A vaccine efficacy of mutant strains of -1.2188, mutant strain recovery rate of -0.8403, and vaccination rate of -0.2578 are the most influential parameters to reduce R_0 . Mutant shedding rate ($\eta_2 = +0.2237$), recruitment rate ($\Lambda = +0.2681$) and mutant strain transmission rate ($\beta_2 = +0.6996$), however, are the strongest drivers of disease spread. Numerical simulations with MATLAB's solver ode45 show that the infection prevalence and environmental bacterial concentration decrease by incorporating increased vaccination coverage and higher vaccine efficacy, hygiene compliance, and sanitation effort. Together with higher transmission rates, higher rate of bacterial shed and mutation rates increase disease persistence. Overall, the study finds an integrated approach to cholera control through a combination of vaccination, treatment, hygiene promotion, environmental sanitation, and pathogen surveillance to be crucial for achieving sustainable results in Kenya. Policy recommendations are given to optimize resource allocation in several different intervention pathways.

MSC2010 Subject Classification: Primary: 92D30, Secondary: 34D20, 34A34

Keywords: Sensitivity analysis, numerical simulation, cholera, vaccination, pathogen mutation, intervention strategies, Kenya

1 Introduction

The outbreaks have become common in Kenya, creating a significant public health problem, affecting the country's healthcare system and economy [20]. Even with vaccination drives, sanitation efforts and public education, cholera continues to break out in various areas—and in the migrant slums, refugee camps, and flood hazard areas [20]. This disease has had a devastating effect despite the efforts of control; therefore, it is desirable to have a quantitative assessment of the relative effectiveness of the various types of control.

Mathematical modelling has proven to be helpful when evaluating the effects of varying intervention strategies [21] and has been applied to evaluate cholera intervention strategies. The various control measures have been investigated in the context of modelling involving compartmentalised models which involve the consideration of environmental bacterial reservoir, the vaccination dynamics and the sanitation interventions [4, 8, 13]. To identify those parameters that have the greatest influence on the spread of the disease, sensitivity analysis techniques have been applied and this will guide which programs will be prioritised for public health use in allocating resources for public health interventions [7, 18].

But most recent sensitivity analysis of cholera model takes individual factors into consideration without the inter-dependence of the factors [13, 4]. Moreover, in the background of vaccine escape and antimicrobial resistance, only few studies have incorporated the pathogen mutation between the wild type and mutant strain in the sensitivity analysis methods. In addition, with the increasing evidence of vaccine escape and antimicrobial resistance, there are still few studies that incorporated the mutation of the pathogen between the wild type and the mutant strains in sensitivity analysis methods.

This paper aims to cut down on these gaps by performing a detailed sensitivity analysis and numerical simulations on a deterministic cholera transmission model that includes vaccination, bi-directional mutation of the pathogen, environmental transmission, sanitation, and compliance with hygiene practices. In this paper we compute the basic reproduction number, determine the equilibrium points and derive the conditions for their stability. This paper will concentrate on the:

1. Creation of normalized forwards sensitivity indices for all the model variables to determine which one has the most influence on the R_0 ; and
2. Mathematical modelling of the disease dynamics to explore the influence from disease control parameters; Compare the effectiveness of vaccine, medicine, hygiene, sanitation and protection of environment;
3. Making quantitative recommendations on integrated cholera control in Kenya.

2 Model Summary

The derivation of the full model, analysis of its equilibrium and stability argument have been studied. In summary, for completeness the model equations and values of parameters used in this analysis are presented.

2.1 Model Equations

The deterministic compartmental model is a model that partitions the human population into different compartments: susceptible (S), vaccinated (V), wild-type infected (I_1), mutant infected (I_2), and recovered (R), and introduces an environmental bacterial concentration (B). The following are model equations:

$$\begin{aligned}\frac{dS}{dt} &= \Lambda - (\lambda_1 + \lambda_2)S - \xi S + \rho V + \omega R - \mu S, \\ \frac{dV}{dt} &= \xi S - (1 - \epsilon_1)\lambda_1 V - (1 - \epsilon_2)\lambda_2 V - \rho V - \mu V, \\ \frac{dI_1}{dt} &= \lambda_1(S + (1 - \epsilon_1)V) + m_{21}I_2 - (\gamma_1 + \alpha_1 + \mu + m_{12})I_1, \\ \frac{dI_2}{dt} &= \lambda_2(S + (1 - \epsilon_2)V) + m_{12}I_1 - (\gamma_2 + \alpha_2 + \mu + m_{21})I_2, \\ \frac{dR}{dt} &= \gamma_1 I_1 + \gamma_2 I_2 - (\omega + \mu)R, \\ \frac{dB}{dt} &= (1 - \kappa_S)\eta_1 I_1 + (1 - \kappa_S)\eta_2 I_2 - (\delta + \kappa_S)B,\end{aligned}\tag{1}$$

where the forces of infection are:

$$\lambda_i = (1 - \kappa_H)\beta_i \frac{I_i}{N} + \beta_{E,i} \frac{B}{K + B}, \quad i = 1, 2.\tag{2}$$

2.2 Parameter Values

The initial set of values for the various parameters, adopted for the simulations, are listed in Table 1. The values are retrieved from literature and representative of the cholera transmission conditions in Kenya.

Table 1: Model Parameters, Descriptions, Baseline Values and Sources

Symbol	Description	Baseline Value	Source
Λ	Recruitment rate into susceptible population	0.55 day^{-1}	[11]
μ	Natural mortality rate	$4.5 \times 10^{-5} \text{ day}^{-1}$	[11]
ξ	Vaccination rate	0.005 day^{-1}	[4]
ϵ_1	Vaccine efficacy against wild strain	0.85	[4]
ϵ_2	Vaccine efficacy against mutant strain	0.70	Assumed
ρ	Vaccine waning rate	0.0011 day^{-1}	[?, 15]
ω	Natural immunity waning rate	0.0005 day^{-1}	[?]
β_1	Human-to-human transmission coefficient for strain 1	0.25 day^{-1}	[11, 22]
β_2	Human-to-human transmission coefficient for strain 2	0.30 day^{-1}	Assumed
$\beta_{E,1}$	Environmental transmission coefficient for strain 1	0.15 day^{-1}	[6, 17]
$\beta_{E,2}$	Environmental transmission coefficient for strain 2	0.18 day^{-1}	Assumed
K	Half-saturation constant	$1.0 \times 10^6 \text{ cells/ml}$	[6, 11]
γ_1	Recovery rate from strain 1 infection	0.20 day^{-1}	[22]
γ_2	Recovery rate from strain 2 infection	0.18 day^{-1}	Assumed
α_1	Disease-induced mortality rate for strain 1	0.010 day^{-1}	[11]
α_2	Disease-induced mortality rate for strain 2	0.015 day^{-1}	Assumed
m_{12}	Mutation rate from strain 1 to strain 2	0.002 day^{-1}	[12]
m_{21}	Mutation rate from strain 2 to strain 1	0.001 day^{-1}	[12]
η_1	Bacterial shedding rate by strain 1 infected individuals	$10 \text{ cells ml}^{-1} \text{ day}^{-1}$	[9, 10]
η_2	Bacterial shedding rate by strain 2 infected individuals	$12 \text{ cells ml}^{-1} \text{ day}^{-1}$	Assumed
δ	Natural bacterial decay rate	0.23 day^{-1}	[6, 11]
κ_S	Sanitation effort parameter	0.10	Assumed
κ_H	Hygiene compliance parameter	0.10	Assumed

Table 2: Initial conditions used in numerical simulations

Variable	Initial Condition
$S(0)$	5000
$V(0)$	1500
$I_1(0)$	6
$I_2(0)$	6
$R(0)$	0
$B(0)$	500

3 Sensitivity Analysis

3.1 Methodology

Sensitivity analysis was performed to check the relative importance of the model parameters on the basic reproduction number, R_0 . The aim was to determine which parameters of the model were the most important for the dynamics of cholera transmission and use these to guide the intervention strategies.

The normalized forward sensitivity index of R_0 is given for any model parameter p as follows:

$$\Gamma_p^{R_0} = \frac{\partial R_0}{\partial p} \times \frac{p}{R_0}, \quad (3)$$

R_0 is the basic reproduction number and p is the parameter of interest. The sensitivity index quantifies by how much R_0 increases when the value of the corresponding parameter increases by one percent, while the value of the other parameters remains fixed.

Positive sensitivity index means that an increase in the parameter leads to an increase in the basic reproduction number, which leads to increased transmission of disease. If the sensitivity index is negative, then an increase in the parameter leads to a decrease of the basic reproduction number, which also contributes to disease control.

Together with the parameter values listed in Table 1 the expression for R_0 obtained has been inserted into MATLAB. A MATLAB program was used to numerically determine the basic reproduction number and the normalized forward sensitivity index for each parameter. The sensitivity indices are then presented in order of their magnitudes.

The basic reproduction number was determined for the parameter values given in Table 1 to be:

$$R_0 = 0.78398. \quad (4)$$

3.2 Sensitivity Analysis Results

Table 3 shows the normalized forward sensitivity indices of all the model parameters. The parameters are ordered according to the size of their sensitivity indices.

Table 3: Sensitivity indices of the basic reproduction number R_0 .

Parameter	Sensitivity Index
ϵ_1	-0.1719
ϵ_2	-1.2188
κ_H	-0.0813
γ_1	-0.0738
γ_2	-0.8403
Λ	0.2681
κ_S	-0.1106
δ	-0.1854
β_2	0.6996
β_1	0.0335
$\beta_{E,2}$	0.2230
$\beta_{E,1}$	0.0449
ξ	-0.2578
η_2	0.2237
ρ	0.2493
η_1	0.0442
α_2	-0.0707
α_1	-0.0038
m_{12}	-0.0031
m_{21}	0.0015
μ	-0.2552
ω	0

3.3 Interpretation of Sensitivity Indices

3.3.1 Parameters with Strong Negative Impact

The mutant strain (ϵ_2) has the highest negative sensitivity index (-1.2188) in terms of vaccine efficacy. This means that with 1

The second highest negative sensitivity index (-0.8403) is for the recovery rate from the mutant strain, γ_2 . This implies that increasing the effectiveness of treatment for infections due to mutant strains would significantly decrease R_0 . Thus, early diagnosis and appropriate treatment protocols are crucial.

This vaccination rate ξ has a negative sensitivity index of -0.2578 : a decrease in vaccination coverage causes a decrease in R_0 . The index of the natural mortality rate μ is negative but not something that can be controlled, $\mu = -0.2552$.

The sensitivity index of the bacterial decay rate δ is -0.1854 which is negative which means that an increase of the natural decay of bacteria in the environment will result in a decrease in R_0 . The negative index of -0.1106 for sanitation effort, κ_S indicates that transmission is reduced by environmental sanitation. The compliance with hygiene conditions, κ_H , has a negative index of -0.0813 indicating that better hygiene behaviours also lead to lower R_0 .

3.3.2 Parameters that have a strong positive effect

The highest positive sensitivity index (+0.6996) is found for the rate of mutant strain transmission β_2 . Therefore, an increase in mutant transmission of 1% will result in an increase of about 0.70% of R_0 . This highlights the need to specifically control the mutant strain.

The recruitment rate, Λ has a positive sensitivity index of +0.2681 meaning that the growth of the susceptible pool of people will contribute to the spread of the disease with an increase in the recruitment.

The vaccine waning rate, ρ , has a positive sensitivity index of +0.2493 indicating that a higher loss rate of vaccine induced immunity is associated with a higher R_0 . This is an example of the importance of vaccine durability.

The mutant strain shedding rate, η_2 has a positive index of +0.2237 while the environmental transmission rate for the mutant strain, $\beta_{E,2}$, has a positive index of +0.2230. These results underline the importance of environment contamination in the transmission of cholera, especially the mutant ones.

3.3.3 Parameters that are insensitive to changes in the design

The mutation parameters, m_{12} and m_{21} , have relatively low sensitivity indices (−0.0031 and +0.0015, respectively). This indicates that mutation affects the make-up of infected populations, but has only limited direct impact on the invasion threshold R_0 . Similarly, mutation can still have a considerable impact on the ratio of wild-type to mutant infections, and long-term disease dynamics, respectively.

The natural immunity waning rate ω has a sensitivity of zero for the baseline values of the other parameters, meaning that there is no direct effect of this parameter to R_0 for the baseline parameters.

4 Numerical Simulation Methodology

4.1 Numerical Method

Numerically, the system of nonlinear ordinary differential equations (1) was solved numerically via the built-in function ode45 of the computer program MATLAB, which is a Runge–Kutta integration scheme of 4th order with adaptive step size. All the simulations were performed with the same set of parameter values as given in Table 1 and values of initial conditions in Table 2.

One factor at a time sensitivity analysis approach was employed to investigate the influence of each parameter on the transmission of cholera. For each of the simulations, the parameter that was varied was within a range of biologically plausible values, and all other parameters were fixed at their baseline values. For the numerical experiments a fixed time interval was chosen to analyse the temporal dynamics of the various compartments.

4.2 Simulation Scenarios

Simulations were conducted to investigate the effects of: vaccination rate (ξ), vaccine efficacy (ϵ_1, ϵ_2), vaccine waning rate (ρ), transmission rates (β_1, β_2), environmental transmission rates ($\beta_{E,1}, \beta_{E,2}$), recovery rates (γ_1, γ_2), hygiene compliance (κ_H), sanitation effort (κ_S), bacterial shedding rates (η_1, η_2) and bacterial decay rate (δ).

4.2.1 Dynamics of Susceptible Individuals

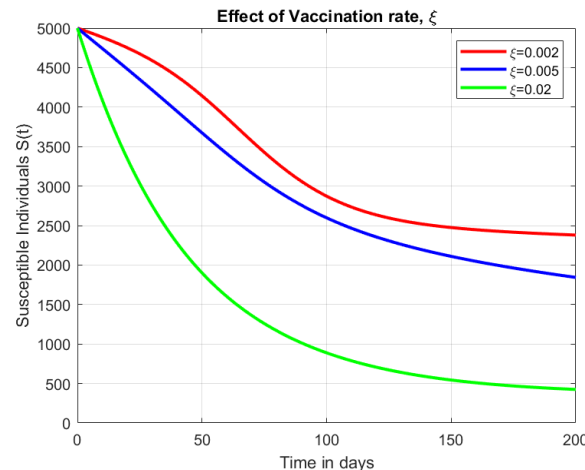


Figure 1: Effects of vaccination rates on susceptible individuals.

Figure 1 above shows the effects of changing the vaccination rate, ξ from its initial value of $\xi = 0.005$ on the susceptible population. As can be seen above, the increase in ξ decreases the number of the susceptible individuals over time since more individuals enter the vaccinated state while the reverse is true for low vaccination rate. It means that increased vaccination is efficient in reducing the population at risk of cholera infection. The observed response correlates with the flow from susceptible to vaccinated compartment, that increases with ξ . Therefore, increasing vaccination rates decreases the number of people who are not vaccinated.

4.2.2 Dynamics of Vaccinated Individuals

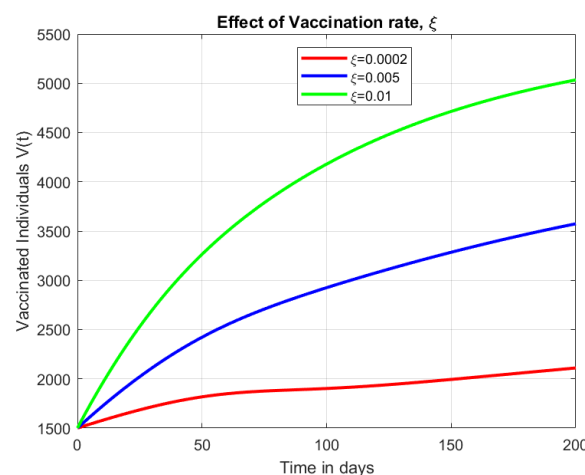


Figure 2: Effects of vaccination rate ξ on vaccinated individuals.

Figure 2 above shows the effect of changing the vaccination rate, ξ from its initial value of $\xi = 0.005$ on the vaccinated population. From the figure, it is clear that the increase in the vaccination rate, ξ increases the number of the vaccinated individuals since more susceptible individuals become

vaccinated. Low vaccination rates lead to small vaccinated population and hence increased population immunity. The vaccinated population is thus a direct function of changes in the vaccination rate.

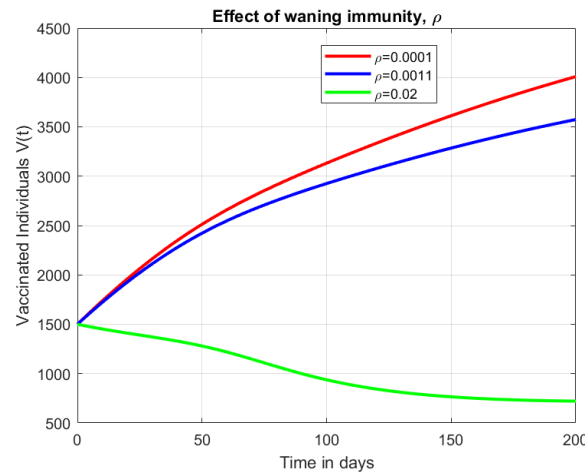


Figure 3: Effect of waning immunity ρ on vaccinated individuals.

Figure 3 above shows the effects of changing the waning immunity rate, ρ from its initial value of $\rho = 0.0011$ on the vaccinated population. The effect of high waning immunity rate is that it decreases the vaccinated population since immunity is lost very fast and vaccinated individuals revert back to the susceptible state. Low waning immunity rates keep the vaccine induced immunity for longer times and therefore, it is necessary to have a vaccine with high lasting effect for controlling cholera.

4.2.3 Dynamics of Individuals Infected with Wild-Type Strain

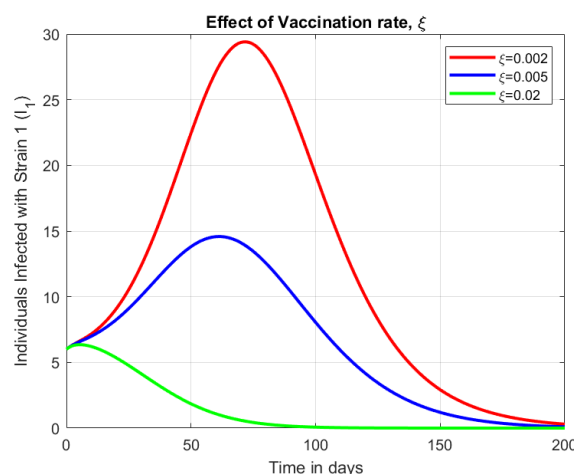


Figure 4: Effect of vaccination rate ξ on individuals infected with wild type strain(I_1).

Figure 4 above shows the effect of varying the vaccination rate ξ on the wild type strain(I_1). Increasing ξ from 0.005 to higher levels reduces the number of individuals infected with the wild-type strain, as

a larger proportion of of the susceptible population is protected through vaccine-induced immunity. Conversely, reducing vaccination rates allow the disease to persist increasing the number of individuals infected with the wild-type strain due to failure of achieving sufficient herd immunity.

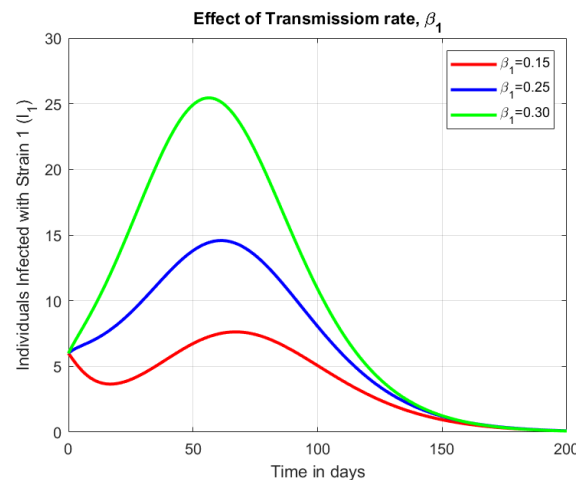


Figure 5: Effect of transmission rate β_1 on individuals infected with wild type strain(I_1).

Figure 5 below shows the influence of the human-to-human transmission parameter β_1 on wild-type infections. From the sensitivity analysis results, the value of the parameter β_1 has a positive sensitivity index (+0.0335). Therefore, lowering the parameter will lower the value of the basic reproduction number R_0 . This shows the need for non-pharmacological measures to lower the force of infection.

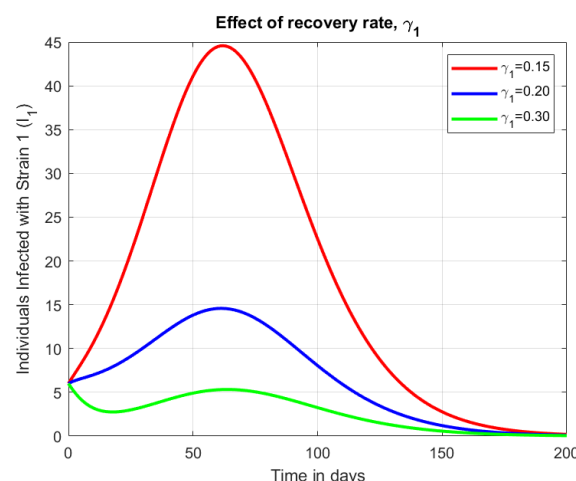


Figure 6: Effect of recovery rate γ_1 on individuals infected with wild type strain(I_1).

Figure 6 shows the effect of the recovery rate γ_1 on wild-type infections. Higher recovery rates shorten the infectious period, reducing the opportunity for onward transmission. The sensitivity analysis confirms γ_1 has a negative sensitivity index (-0.0738), indicating that improving recovery rates through effective treatment reduces R_0 and helps control the disease. It also defines the speed with which people transition from the compartment of wild-type infection to the recovered compartment.

This emphasizes the need for prompt diagnosis and case management to accelerate recovery.

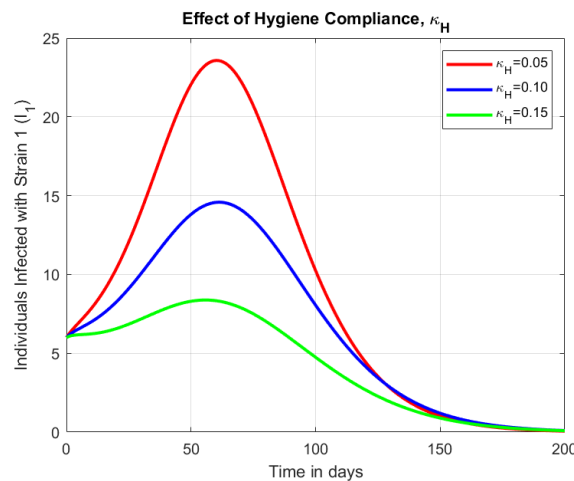


Figure 7: Effect of hygiene compliance κ_H on individuals infected with wild type strain(I_1).

Figure 7 above shows the effects of changing the hygiene compliance rate, κ_H from its initial value of $\kappa_H = 0.10$. The effect of high hygiene compliance rate on the infected individuals is that it decreases the number of individuals infected since it reduces disease transmission. Poor hygiene compliance results in large outbreaks and hence, hygiene intervention is efficient in controlling cholera prevalence.

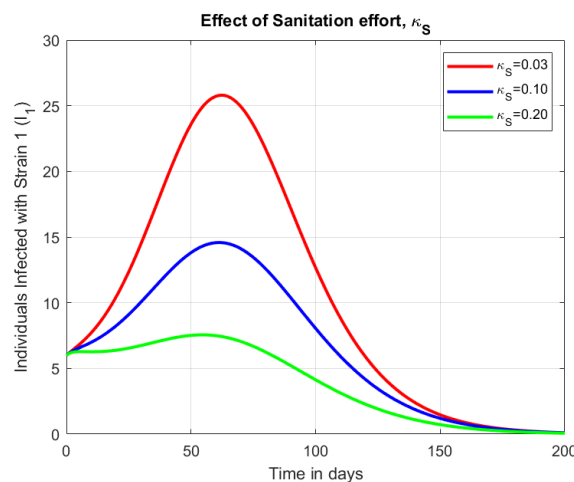


Figure 8: Effect of sanitation effort κ_S on individuals infected with wild type strain(I_1).

Figure 8 above shows the effects of varying the sanitation effort, κ_S from its initial value of $\kappa_S = 0.10$ on individuals infected with the wild type strain. From the figure above, we observe that the number of individuals infected with the wild type strain reduces with an increase in sanitation efforts because more bacteria are removed from the environment while low sanitation efforts lead to high environmental contamination and therefore higher numbers of infected individuals. This implies that sanitation is effective in controlling the spread of the wild type strain.

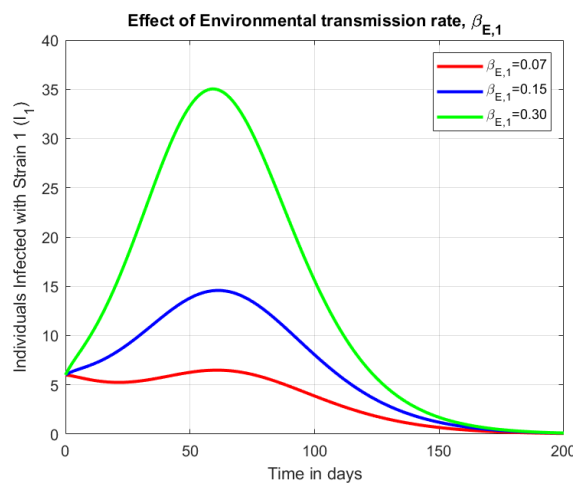


Figure 9: Effect of Environmental transmission rate $\beta_{E,1}$ on individuals infected with wild type strain(I_1).

Figure 9 above shows the effects of varying the environmental transmission rate, $\beta_{E,1}$ from its initial value of $\beta_{E,1} = 0.15$ on individuals infected with the wild type strain. From the figure above, we observe that the number of infected individuals increases with an increase in the environmental transmission rate since more susceptible individuals get infected through the environment while the opposite is the case for low environmental transmission rates. It implies that reducing environmental transmission is important in controlling the spread of cholera infection.

4.2.4 Dynamics of Individuals Infected with Mutant Strain

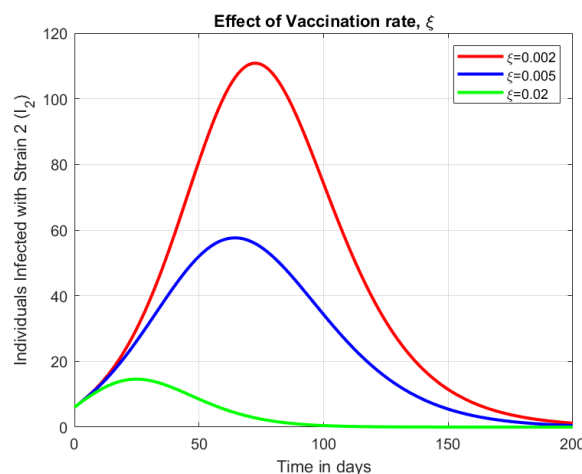


Figure 10: Effect of vaccination rate ξ on individuals infected with mutant strain(I_2).

Figure 10 above shows the effect of varying the vaccination rate ξ on the mutant strain(I_2). Increasing ξ from 0.005 to higher levels reduces the number of individuals infected with the mutant strain(I_2), as a larger proportion of of the susceptible population is protected through vaccine-induced immunity.

Conversely, reducing vaccination rates allow the disease to persist increasing the number of individuals infected with the mutant strain(I_2) due to failure of achieving sufficient herd immunity.

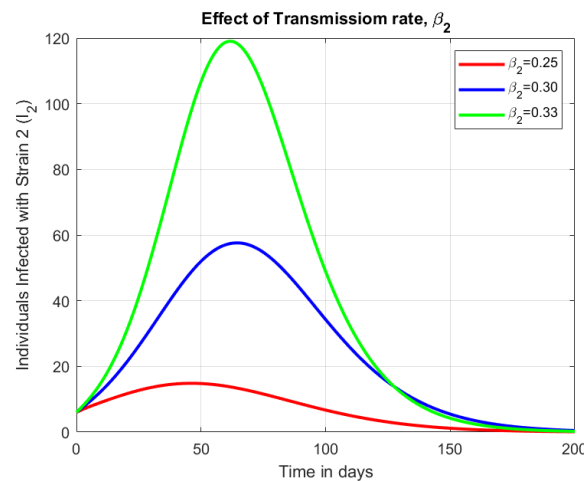


Figure 11: Effect of transmission rate β_2 on individuals infected with mutant strain(I_2).

Figure 11 illustrates the effect of the transmission rate β_2 on mutant strain infections. The mutant strain has a higher baseline transmission rate ($\beta_2 = 0.30$) than the wild-type strain ($\beta_1 = 0.25$). The sensitivity analysis confirms β_2 has the highest positive sensitivity index (+0.6996), meaning it is the most influential parameter in increasing R_0 . As the mutant strain of the virus is directly controlled by β_2 , any change in β_2 results in a direct effect on the new mutant infection. This underscores the critical need for transmission-reducing interventions specifically targeting the mutant strain.

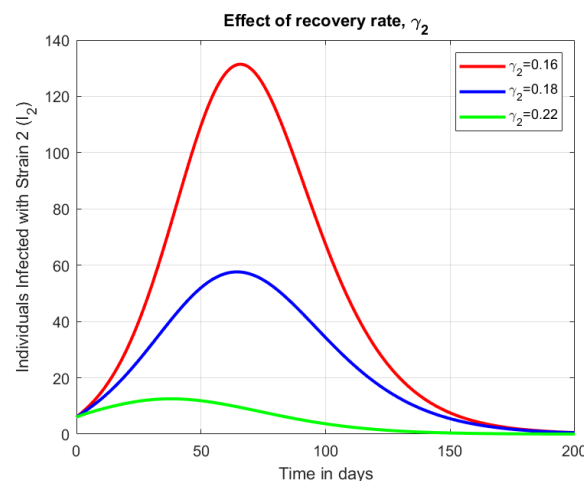


Figure 12: Effect of recovery rate γ_2 on individuals infected with wild type strain(I_2).

Figure 12 shows the effect of the recovery rate γ_2 on mutant strain infections. The mutant strain has a lower recovery rate ($\gamma_2 = 0.18$) than the wild-type strain ($\gamma_1 = 0.20$), prolonging the infectious period and contributing to its persistence. The sensitivity analysis confirms γ_2 has the second highest negative

sensitivity index (-0.8403), indicating that improving recovery rates through effective treatment is critical for controlling the mutant strain. This highlights the need for treatment protocols that are effective against both strains.

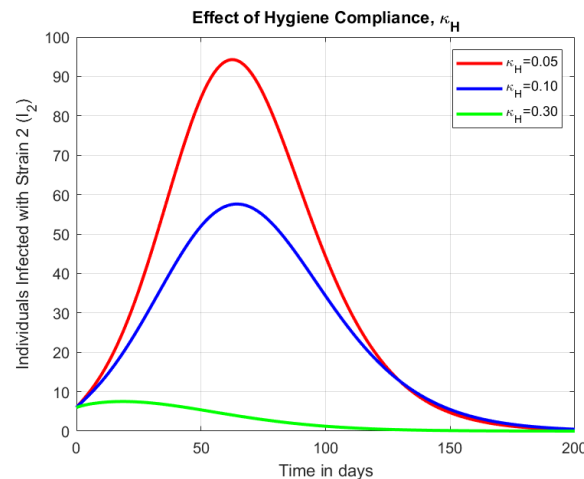


Figure 13: Effects of Hygiene compliance κ_H on individuals infected with mutant strain(I_2).

Figure 13 above shows the effects of varying the hygiene compliance, κ_H from its initial value of $\kappa_H = 0.10$ on individuals infected with the mutant strain. From the figure above, we observe that the number of infected individuals decreases with an increase in hygiene compliance since disease transmission is reduced while the opposite is the case for low hygiene compliance. This implies that hygiene compliance is important in controlling the spread of the mutant strain.

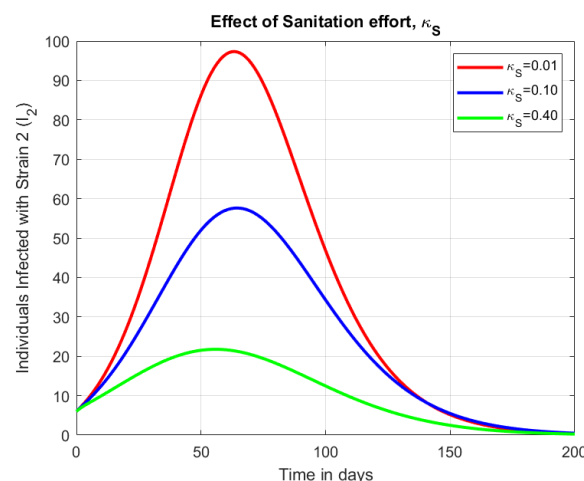


Figure 14: Effects of Sanitation effort κ_S on individuals infected with mutant strain(I_2).

Figure 14 above shows the effects of varying the sanitation effort, κ_S from its initial value of $\kappa_S = 0.10$ on individuals infected with the mutant strain. From the figure above, we observe that the number of infected individuals decreases with an increase in sanitation efforts because more bacteria are removed

from the environment while the opposite is the case for low sanitation efforts. This implies that improved sanitation is important in controlling the spread of the mutant strain.

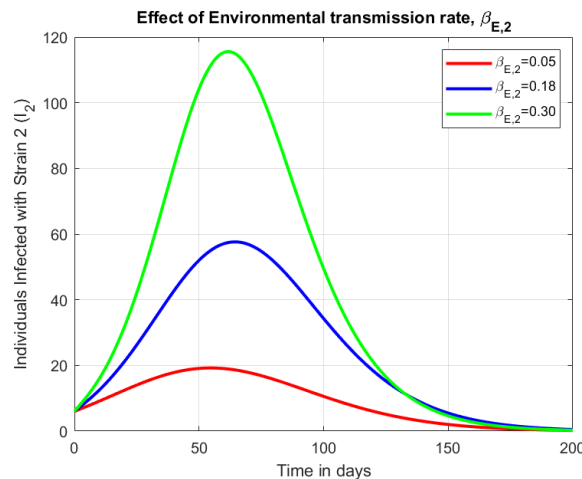


Figure 15: Effects of Environmental transmission rate $\beta_{E,2}$ on individuals infected with mutant strain(I_2).

Figure 15 above shows the effects of varying the environmental transmission rate, $\beta_{E,2}$ from its initial value of $\beta_{E,2} = 0.18$ on individuals infected with the mutant strain. From the figure above, we observe that the number of infected individuals increases with an increase in the environmental transmission rate since more susceptible individuals get infected through the environment while the opposite is the case for low environmental transmission rates.

4.2.5 Dynamics of Recovered Individuals

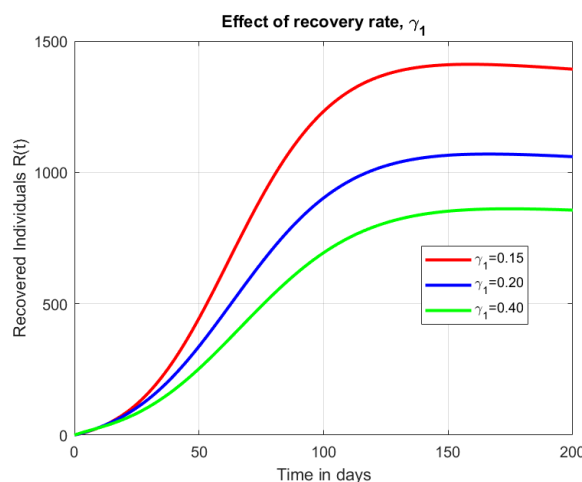


Figure 16: Effects of recovery rate γ_1 on recovered individuals.

The impact of changes in the value of the recovery rate γ_1 from its value $\gamma_1 = 0.20$ on the recovered

population is shown in Figure 16 above. An increased recovery rate means a quicker recovery period, where infected people stay in the infected class for a shorter period before moving to the recovered class, thus leading to a reduced peak of recovered people at any one time. On the other hand, a reduced recovery rate increases the period that infected people remain infected, thus leading to more accumulation in the infected class until they finally move to the recovered class, hence an increase in the number of recovered people over time. The green line represents the lowest recovered people because they recover quickly and move through the recovered class, while the red line represents the highest number of recovered people because they take a longer time to recover and accumulate in the recovered class.

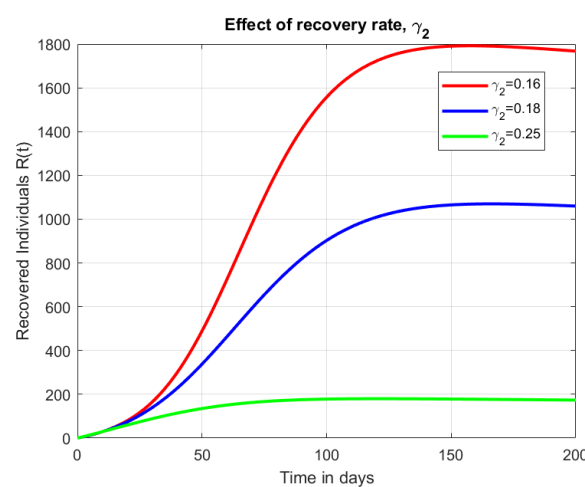


Figure 17: Effects of recovery rate γ_2 on recovered individuals.

In Figure 17 above, the impact of varying the recovery rate, γ_2 from $\gamma_2 = 0.18$ is illustrated in terms of the recovered population. The effect of increased recovery rate means that there will be quicker recovery, which translates to less time spent in the recovered state. It implies that there will be less build-up of recovered individuals since they leave the state quickly. Inversely, the low recovery rate implies that there will be prolonged infection, hence leading to increased recovered individuals due to time spent in the recovered category. As depicted in Figure 4.17 above, the green line represents the minimum recovered population since the individuals recover quickly from the infected state into the recovered category.

4.2.6 Dynamics of Environmental Bacteria

Figure 18 above shows the effects of changing the shedding rate of strain one, η_1 from its initial value of $\eta_1 = 10$ on the environmental bacteria. High shedding rate increases environmental bacteria concentration since more bacteria are shedded into the environment by the infected individuals. Therefore, changes in η_1 directly affect the number of bacteria that will be added to the environmental compartment.

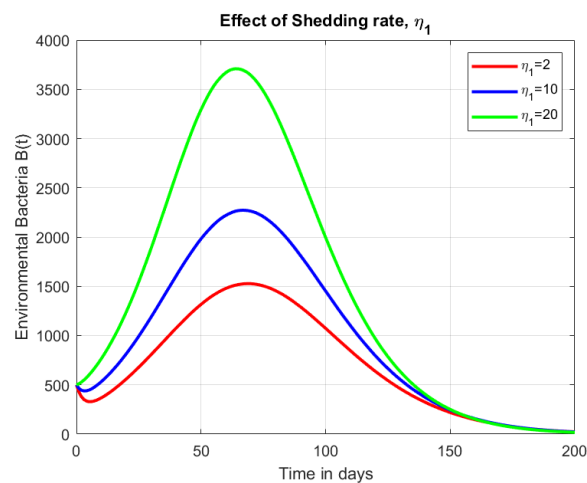


Figure 18: Effects of shedding rate η_1 on Environmental Bacteria.

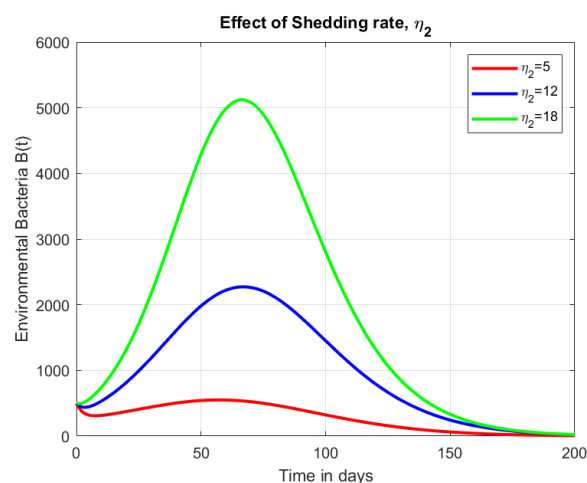


Figure 19: Effects of shedding rate η_2 on Environmental Bacteria.

Figure 19 above shows the effects of changing the shedding rate of strain two, η_2 from its initial value of $\eta_2 = 12$ on the environmental bacteria. Increased shedding rate increases environmental bacteria concentration since more bacteria are shedded into the environment. Thus, the larger the η_2 the larger the bacterial input from strain 2.

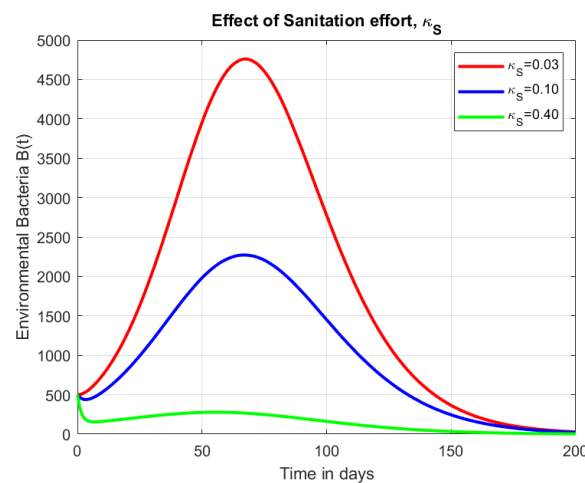


Figure 20: Effects of sanitation effort κ_S on Environmental Bacteria.

Figure 20 above shows the effect of changing the sanitation effort, κ_S from its initial value of $\kappa_S = 0.10$ on the environmental bacteria. High sanitation efforts reduce the environmental bacteria concentration since more bacteria are removed from the environment. Sanitation has both impacts on the environmental bacterial population, firstly is a reduction of bacterial input and secondly is an increase of bacterial removal. As a result, the more sanitized a product is, the fewer bacteria will be present.

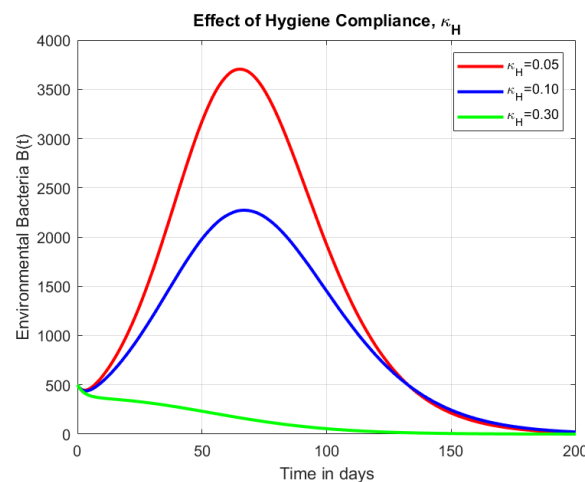


Figure 21: Effects of Hygiene compliance κ_H on Environmental Bacteria.

Figure 21 above shows the effect of changing the hygiene compliance, κ_H from its initial value of $\kappa_H = 0.10$ on the environmental bacteria. High hygiene compliance reduce the environmental bacteria concentration since more bacteria are removed from the environment. The impact of hygiene compliance on the environmental bacteria is primarily indirect as it affects infection and subsequently shedding of bacteria. If compliance can be improved, the amount of bacteria that can be transferred by infected individuals can also be reduced.

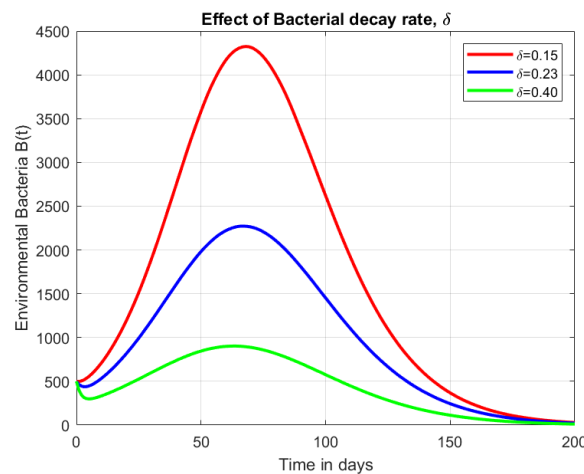


Figure 22: Effects of Bacterial decay rate δ on Environmental Bacteria.

Figure 22 above shows the effect of changing the bacterial decay rate, δ from its initial value of $\delta = 0.23$ on the environmental bacteria. High bacterial decay rate reduce the environmental bacteria concentration since more bacteria are die off from the environment. Therefore, the greater the value of δ the lower the persistence of bacteria in the environment.

5 Discussion and Conclusion

5.1 Analysis Conclusion

A deterministic mathematical model which described the transmission dynamics of cholera in the presence of vaccination, pathogen mutation, environmental contamination, sanitation intervention and hygiene compliance was developed and analyzed in this study. The purpose of developing this model was to analyze the role of vaccination and environmental control measures on the spread and persistence of cholera within a population.

The positivity and boundedness of the solution of the model was proved thereby showing that the model is well-posed from both mathematical and epidemiological points of view. It was proved that all state variables are always non-negative for all future time under non-negative initial conditions. Moreover, the feasible region

$$\Omega = \left\{ (S, V, I_1, I_2, R, B) \in \mathbb{R}_+^6 : N(t) \leq \frac{\Lambda}{\mu} \right\}$$

is positively invariant showing that all solutions of the model are biologically meaningful throughout the course of the disease transmission.

The disease-free equilibrium point

$$E_0 = (S^*, V^*, 0, 0, 0, 0)$$

was obtained and analyzed. Using the next-generation matrix approach, the basic reproduction number R_0 was calculated and identified as the threshold parameter that determines the dynamics of the disease. It was shown that the disease-free equilibrium point is locally asymptotically stable whenever

$$R_0 < 1,$$

and unstable whenever

$$R_0 > 1.$$

This means that the transmission dynamics of cholera cannot persist within the population if R_0 is kept below one.

Moreover, the endemic equilibrium point was obtained by solving the steady state system generated from the model equations. The analysis shows that the endemic equilibrium point exists if and only if $R_0 > 1$ thereby implying that cholera will persist within the population if R_0 is kept above the critical value of one.

Finally, sensitivity analysis was conducted to explore the impact of model parameters on the value of the basic reproduction number. It was observed that vaccine efficacy against both wild and mutant strains, hygiene compliance, recovery rates, sanitation effectiveness and bacterial shedding control have negative normalized forward sensitivity indices with respect to R_0 . This implies that an increase in their values reduces the value of R_0 . On the other hand, transmission coefficients and mutation related parameters were found to have positive sensitivity indices thereby increasing the value of R_0 .

Consequently, the analytical results show that effective control of cholera transmission depends on the interventions that reduce the value of the reproduction number through improvement of vaccination, treatment, sanitation, hygiene compliance and environmental management.

5.2 Simulations Conclusion

The numerical simulations were done by using the baseline parameters presented in Chapter Four in order to validate the analytical results and investigate the effect of selected parameters on the dynamics of the state variables.

From the simulation results, it was observed that an increase in vaccination rate and vaccine efficacy reduces the population of individuals infected with the two strains while increasing the vaccinated population. This implies that an increase in the value of those two parameters will reduce the infection prevalence thereby confirming the analytical result of negative sensitivity index of the basic reproduction number due to vaccine efficacy.

In addition, the simulations were used to investigate the effect of pathogen mutation. From the results, it was noted that an increase in the mutation rate increases the population infected with the mutant strain while reducing the prevalence of the wild strain. Therefore, this shows that mutation influences the persistence of cholera and could affect its long-term epidemiological dynamics.

Also, it was found that increases in hygiene compliance and sanitation effectiveness lead to decreases in the force of infection and environmental bacterial concentration. This is in line with the analytical results of sensitivity indices thereby emphasizing the importance of environmental interventions in controlling cholera transmission.

The influence of bacterial shedding and environmental contamination was also investigated through the simulation results. An increase in bacterial shedding rate leads to increase in environmental contamination while an improvement in their removal mechanisms leads to reduction in the level of disease transmission.

Therefore, the numerical results support the theoretical findings obtained from the analytical study. An increase in the value of the parameter that reduces the value of the reproduction number also reduces the prevalence of the disease. In addition, the results show that a combination of different intervention strategies including vaccination, sanitation improvement, hygiene compliance and treatment programmes is more effective in reducing the transmission of cholera compared to isolated intervention methods.

5.3 Recommendations of the Research

The findings of this study suggest that the control of cholera can be achieved by applying intervention strategies that will modify the most sensitive parameters of the model. Since the sensitivity analysis revealed that vaccine efficacy, hygiene compliance, recovery rates and sanitation effectiveness have negative effects on the basic reproduction number, efforts should be made to increase the values of the latter parameters. Specifically, increasing the vaccination coverage and the efficacy of the vaccines will reduce the susceptible population thereby decreasing the force of infection. Similarly, improving treatment and case management programmes will increase the recovery rates of the infected individuals and decrease the average infectious period.

Furthermore, the numerical simulations show that improving hygiene practices and sanitation interventions will reduce environmental contamination and disease transmission. Therefore, it is recommended to implement programmes that ensure access to safe water, proper waste disposal and awareness of the community about hygiene issues. Also, surveillance systems should be strengthened in order to detect mutant cholera strains and prevent their spread since mutation dynamics was found to be one of the factors affecting the persistence of cholera. In general, the study recommends that control of cholera will depend on integrated intervention strategies which will combine vaccination, treatment, sanitation and hygiene interventions in order to achieve sustainable reduction of the disease transmission and keep the reproduction number below the epidemic threshold.

5.4 Suggestions for Future Research

Even though the model provided some insights into the transmission dynamics of cholera, there are some possible extensions that could be done in future researches. First of all, the current work focused mainly on the local stability properties of the equilibria and, therefore, future research can consider investigating the global asymptotic stability of both the disease-free and endemic equilibrium points using Lyapunov functions.

Furthermore, the current model assumes homogeneously mixed population and constant parameter values. Therefore, future studies can incorporate the spatial heterogeneity and population mobility in order to better describe transmission patterns. Since random environmental fluctuations can affect the

outbreaks of the disease, stochastic models could also be developed and analyzed. Moreover, optimal control techniques could be incorporated into the model in order to identify cost effective intervention strategies involving vaccination, treatment, sanitation and hygiene measures. Finally, future studies can consider parameter estimation and model validation based on the real epidemiological data.

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