Journal of Mathematical Problems, Equations and Statistics

E-ISSN: 2709-9407
P-ISSN: 2709-9393
JMPES 2024; 5(2): 126-130

www.mathematicaljournal.com
Received: 13-10-2024
Accepted: 15-11-2024

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The effectiveness of multiple control measures for cholera outbreaks in Nigeria using mathematical modeling

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Abstract
Cholera remains a significant global public health burden, particularly affecting regions with inadequate water and sanitation infrastructure. Effective control measures are crucial for mitigating cholera outbreaks and transmission. This study employs mathematical modeling to evaluate the combined effectiveness of multiple interventions - sanitation, treatment, vaccination, and public health education campaigns - in managing cholera dynamics in Nigeria. A new compartmental model is developed that incorporates these control strategies simultaneously. The model tracks susceptible, infected, and recovered populations, as well as the concentration of Vibrio cholerae bacteria in the environment. Specific parameters represent the impact of each intervention, such as reduced susceptibility through vaccination, lowered exposure via education, increased recovery with treatment, and reduced bacterial concentration through sanitation measures. Analysis at the disease-free equilibrium provides insights into the relative influence of these factors. Time-series simulations demonstrate a synergistic effect, with the integrated implementation of all four control measures leading to a steady linear increase in the recovered population over time. This implies that combined interventions are effective in curbing cholera spread and improving recovery rates.

Keywords: Cholera, mathematical modeling, multiple interventions, integrated control strategies, outbreak management, time-series

1. Introduction

Cholera, an acute intestinal infection caused by the bacterium Vibrio cholerae, continues to pose a significant global health threat, particularly in underdeveloped nations with inadequate water and sanitation infrastructure. The disease is characterized by a short incubation period and can lead to severe dehydration and mortality if left untreated. Given the ongoing challenges posed by cholera outbreaks, there is a pressing need to assess the effectiveness of multiple control measures in containing the spread of the disease [1].

Vibrio cholerae is primarily transmitted through the ingestion of contaminated water or food, with the bacterium thriving in unsanitary conditions. Fecal-oral transmission remains a critical pathway, making communities with poor sanitation vulnerable to cholera outbreaks.

Cholera manifests with a sudden onset of profuse watery diarrhea, vomiting, and muscle cramps. Dehydration ensues rapidly, and in severe cases, can lead to shock and death if left untreated. Rehydration therapy, including the administration of oral rehydration solutions, remains the cornerstone of cholera treatment. Timely medical intervention can significantly reduce mortality rates associated with the disease.

Preventing cholera outbreaks necessitates a multifaceted approach. Improved sanitation and access to clean water are fundamental, disrupting the transmission cycle. Vaccination campaigns, when feasible, offer additional protection. However, the integration of multiple control measures requires careful consideration to enhance effectiveness [1].

Despite ongoing efforts to address the global burden of cholera, the disease remains a significant public health concern, particularly in regions with inadequate water and sanitation infrastructure. Mathematical modeling can provide valuable insights into the potential impact of control measures such as sanitation, treatment, vaccination, and public health education campaigns on cholera transmission dynamics. However, there is a need to evaluate the combined impact of these measures and to consider the complex contextual factors that can influence their effectiveness in real-world settings. Addressing this problem can help to inform the development and implementation of more effective and sustainable control measures for managing cholera outbreaks.

Cholera is a major public health concern in Nigeria, with the country reporting the second-highest number of estimated cholera cases in Africa [2]. The disease is caused by the bacterium Vibrio cholerae and is primarily spread through contaminated food or drinking water [3]. Cholera outbreaks in Nigeria have been linked to various social and environmental factors, including droughts, floods, and poor access to water, sanitation, and hygiene (WASH) [2].

Nigeria's northeast region, which experiences frequent attacks from extremist groups like Boko Haram, has been particularly affected by cholera outbreaks [3]. The violence in the region has hampered authorities' efforts to contain the outbreak, leading to significant mortality and morbidity, especially among children under five [2].

Cholera is a significant public health challenge in Nigeria, with the country reporting the second highest number of cases globally. The Global Task Force on Cholera Control (GTFCC) has set targets to reduce cholera deaths by 90% and eliminate the disease in twenty countries by 2030. However, achieving these targets in Nigeria is currently unlikely at a national level, although some parts of the country may reach the targets by 2030. Regional inequalities, including differences in development, sanitation access, and levels of conflict, pose challenges to achieving the targets. Efforts to reach the targets should focus on improving access to cholera testing, sanitation expansion, poverty alleviation, and urban planning. Modelling studies can inform cholera policy and help identify areas for strengthening the three axes of the GTFCC Roadmap: reporting, response, and coordination [2, 4, 5].

In this study, we aim to develop a mathematical model to capture the key dynamics of cholera transmission, with a specific focus on evaluating the impact of sanitation, treatment, vaccination, and public health education campaigns as control measures [1]. By leveraging mathematical modeling techniques, we seek to quantify the potential advantages of implementing these multiple control measures and to assess their combined effectiveness in mitigating cholera outbreaks.

2. Early Models and Transmission Dynamics

Early models of cholera transmission focused on compartmental models, dividing the population into susceptible, infected, and recovered compartments. A foundation was laid with a SIR model, later adapted for cholera by applying mass-action principles [6]. These models provided a basic understanding of epidemic spread, introducing the concept of the basic reproduction number (R0) – the average number of secondary infections caused by a single infected individual. Subsequent models incorporated environmental reservoirs, seasonality, and different transmission pathways (e.g., person-to-person, waterborne) to capture the dynamic nature of cholera outbreaks [7, 8].

2.1 Predicting Outbreaks and Evaluating Interventions

With advancements in computational power and data availability, models evolved to predict the timing and magnitude of cholera outbreaks. By incorporating real-time data on factors like weather, water quality, and sanitation, models can forecast potential outbreaks with increasing accuracy [9, 10]. This information empowers public health officials to preemptively deploy resources and interventions, mitigating the impact of outbreaks.

Furthermore, models are instrumental in evaluating the effectiveness of various control strategies. Studies have compared the impact of interventions like vaccination campaigns, improved water and sanitation infrastructure, and oral rehydration therapy programs [11, 12]. This comparative analysis allows for evidence-based decision making, optimizing resource allocation and prioritizing interventions based on their predicted impact.

3. Methodology

In order to develop a reliable model for assessing the effectiveness of control measures for Cholera outbreaks, multiple control measures were simultaneously incorporated. This will allow for the assessment of the combined impact of various interventions on controlling cholera outbreaks.

3.1 Model Assumptions and Parameters Symbols

The followings are the assumptions for the study which are; (a) the total population size varies over time; (b) Multiple control measures are implemented concurrently; (c) vaccination targets susceptible individuals; (d) therapeutic treatment is applied to infected individuals; (e) water sanitation reduces the concentration of vibrios; (f) education campaigns are conducted to promote hygiene practices.

The Symbols and Parameters of the study are as follows

- S**:** Susceptible individuals
- I**:** Symptomatically infected individuals
- R**:** Recovered individuals
- B**:** Concentration of Vibrio cholerae in the environment
- Λ**:** Constant rate of hiring people
- μ_h**:** Natural human mortality rate
- d**:** Disease-induced death rate
- α_1**:** Rate of exposure to contaminated food and water
- λ**:** Effective contact rate between individuals (with control measures)
- γ**:** Recovery rate of infected individuals
- ϵ**:** Bacteria shedding rate into the water supply by infected humans
- ϕ**:** Per capita rate at which recovered individuals become susceptible again
- θ**:** Effectiveness of control measures (e.g., vaccination, treatment)
- ψ_e**:** Effectiveness of education campaigns in reducing contact rate
- ω_b**:** Effectiveness of water sanitation in reducing vibrio concentration
- K**:** Maximum per capita growth rate for Vibrio cholerae bacteria
- b**:** Bacterial growth rate
- μ_p**:** Natural death rate of bacteria in the environment

3.2 The Model

The model for the study incorporates the effects of multiple control measures which are:

i) For vaccination: Reduce the rate of susceptible individuals being infected (θS).
ii) For education campaigns: Reduce the rate of contact between infected and susceptible individuals ($\psi_e \alpha_1 S$).
iii) For therapeutic treatment: Increase the rate of recovery ($\theta \gamma I$).
iv) For water sanitation: Reduce the concentration of vibrios in the environment ($\omega_b B$).

3.2.1 Model Definition

A. Susceptible population (S)

$$\frac{dS}{dt} = \Lambda + \phi R - (1 - \psi_e)\lambda S - (\mu_h + \theta)S$$

- **Λ:** Represents the constant rate of hiring people into the susceptible population.
- **ϕR:** Represents the rate at which recovered individuals become susceptible again.
- **$(1-\psi_e)\lambda S$:** Represents the rate of exposure to contaminated sources reduced by the effectiveness of education campaigns (ψ_e).
- **$(\mu_h+\theta)S$:** Represents the total death rate of susceptible individuals, including natural mortality (μ_h) and the rate at which susceptible individuals are vaccinated (θ).

B. Symptomatically infected population (*I*)

$$\frac{dI}{dt} = (1-\psi_e)\lambda S - (\mu_h + d + \gamma\theta)I$$

- **$(1-\psi e)\lambda S$:** Represents the rate at which susceptible individuals become infected, reduced by the effectiveness of education campaigns (ψ_e).
- **$(\mu_h + d + \gamma\theta)I$:** Represents the total death rate of infected individuals, including natural mortality (μ_h), disease-induced mortality (d), and the rate of recovery with therapeutic treatment ($\gamma\theta$).

C. Concentration of Vibrio cholerae (*B*) in the environment

$$\frac{dR}{dt} = b\left(1-\frac{B}{K}\right)B + (1-\psi_e)\epsilon I - (\mu_p + \omega_b)B$$

- **$(1-\frac{B}{K})B$:** Represents the growth rate of Vibrio cholerae in the environment, taking into account the carrying capacity (K) and the effectiveness of water sanitation (ω_b).
- **$(1-\psi e)\epsilon I$:** Represents the shedding rate of bacteria into the water supply by infected individuals, reduced by the effectiveness of education campaigns (ψ_e).
- **$(\mu_p + \omega_b)B$:** Represents the total death rate of Vibrio cholerae in the environment, including natural decay (μ_p) and the effectiveness of water sanitation (ω_b).

D. Recovered population (*R*)

$$\frac{dR}{dt} = \gamma I + \theta S - (\mu_h + \phi)R$$

- **γI:** Represents the rate of recovery of infected individuals with therapeutic treatment (γI).
- **θS:** Represents the rate at which susceptible individuals are vaccinated and become recovered.
- **$(\mu_h + \phi)R$:** Represents the total death rate of recovered individuals, including natural mortality (μ_h) and the rate at which recovered individuals become susceptible again (ϕ).

These equations describe the dynamics of susceptible, infected, recovered individuals, and the concentration of Vibrio cholerae in the environment, considering the effects of multiple control measures on cholera transmission dynamics.

4.1 Model Analysis

The model is analyzed to understand its dynamics, stability, and the impact of multiple control measures on cholera transmission.

Disease-Free Equilibrium (DFE)

We can find the disease-free equilibrium by setting all derivatives equal to zero:

$$\frac{dS}{dt} = \Lambda + \phi R - (1-\psi_e)\lambda S - (\mu_h + \theta)S = 0$$

$$\frac{dI}{dt} = (1-\psi_e)\lambda S - (\mu_h + d + \gamma\theta)I = 0$$

$$\frac{dR}{dt} = b\left(1-\frac{B}{K}\right)B + (1-\psi_e)\epsilon I - (\mu_p + \omega_b)B = 0$$

$$\frac{dR}{dt} = \gamma I + \theta S - (\mu_h + \phi)R = 0$$

Solving these equations will give us the values of S^0, I^0, B^0, and R^0 at the disease-free equilibrium point.

Susceptible Population (S)

- The number of susceptible individuals changes over time due to births (Λ), imports (ϕR), infections ($(1-\psi_e)\ \lambda S$), and natural deaths ($(\mu_h + \theta)S$).
- The equation for the rate of change of susceptible individuals is:

$$\frac{dS}{dt} = \Lambda + \phi R - (1-\psi_e)\lambda S - (\mu_h + \theta)S = 0$$

Solving this equation for S yields:

$$S = \frac{\Lambda + \phi R}{(1-\psi_e)\lambda + \mu_h + \theta}$$

Infected Population (I)

- The number of infected individuals changes due to infections ($(1-\psi_e)\lambda S$) and deaths ($(\mu_h + d + \gamma\theta)I$).
- The equation for the rate of change of infected individuals is:

$$\frac{dI}{dt} = (1-\psi_e)\lambda S - (\mu_h + d + \gamma\theta)I = 0$$

- Substituting the expression for S gives:

$$I = \frac{(1-\psi_e)\lambda}{\mu_h + d + \gamma\theta}\left(\frac{\Lambda + \phi R}{(1-\psi_e)\lambda + \mu_h + \theta}\right)$$

Recovered Population (R)

- The number of recovered individuals changes due to recoveries (γI), susceptible individuals becoming recovered (θS), and deaths ($\mu_h+\phi)R$).
- The equation for the rate of change of recovered individuals is:

$$\frac{dR}{dt} = \gamma I + \theta S - (\mu_h + \emptyset)R = 0$$

- Substituting the expression for S and I gives:

$$R = \frac{\gamma}{\mu_h + \emptyset}\left(\frac{(1-\psi_e)\lambda}{\mu_h + d + \gamma\theta}\right)\left(\frac{\Lambda + \phi R}{(1-\psi_e)\lambda + \mu_h + \theta}\right) + \frac{\theta}{\mu_h + \phi}\left(\frac{\Lambda + \phi R}{(1-\psi_e)\lambda + \mu_h + \theta}\right)$$

Birth Rate (B)

- The number of births changes due to birth rate (b), the carrying capacity (KB), infected individuals $(1-\psi_e)\epsilon I$, and deaths ($(\mu_p+\omega_b)B$).
- The equation for the rate of change of the birth population is:

$$\frac{dB}{dt} = b(1 - K_B)B + (1 - \psi_e)\epsilon I - (\mu_p + \omega_b)B = 0$$

- Solving this equation for B yields:

$$B = \frac{(1-\psi_e)\epsilon I}{\mu_p+\omega_b} + \frac{b(1-K_B)}{\mu_p+\omega_b}$$

4.2 Simulation Analysis Using R

Suppose the birth rate Λ (Lambda) is 100; import rate ϕ (phi) = 0.1; disease-induced death rate ψ_e (psi_e) = 0.2; infection rate λ (lambda) = 0.03; natural death μ_h (mu_h) = 0.02; recovery rate θ (theta) = 0.01; recovery rate from infection to immunity γ (gamma) = 0.05; death rate due to infection d (d) = 0.01; probability of infection leading to birth ϵ (epsilon) = 0.1 ; death rate in birth population μ_p (mu_p) = 0.02 ; death rate due to other causes in birth population ω_b (omega_b) = 0.01; base birth rate b (b) =150; carrying capacity factor KB (K_B) = 0.8.

Using R programming to analyze the data above, gave a time series plot of the recovered population over a period of time shown in figure 1.

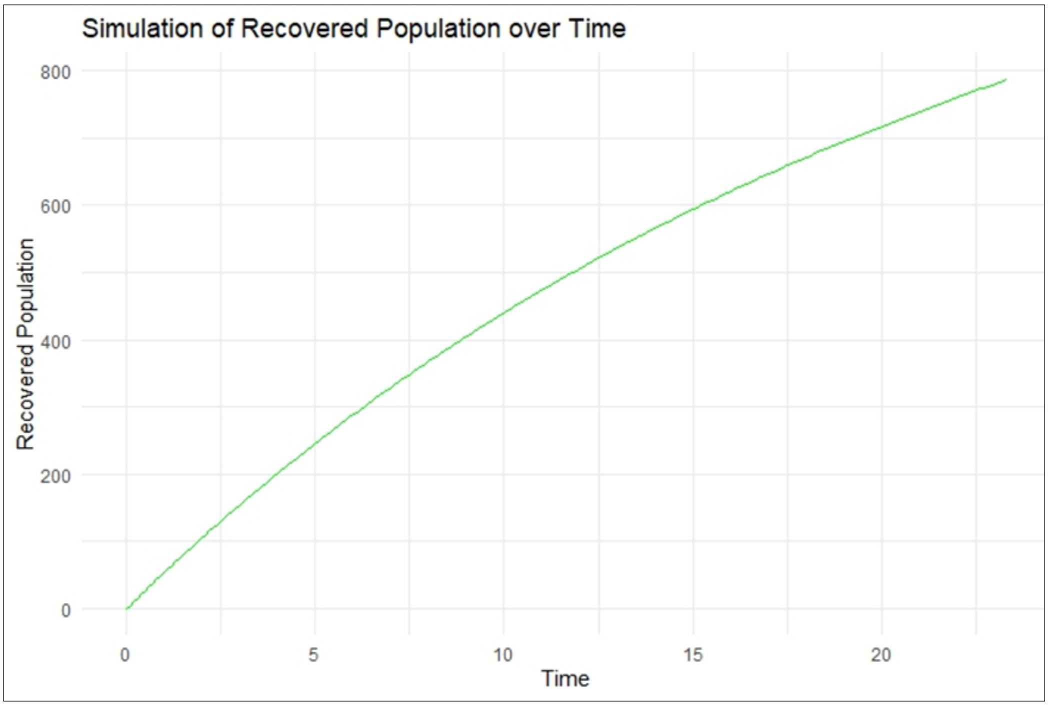

Fig 1: The Time Series plot above shows the recovered population over a period of time.

From the time series plot, the x-axis represents time (in days) and the y-axis represents the recovered population. The upward trend indicates that the integrated impact of vaccination, education campaigns, therapeutic treatment, and water sanitation is effective in increasing the rate of recovery among infected individuals. The sustained rise in the recovered population implies that the measures are successfully mitigating the spread of cholera.

Disease Free Equilibrium (DFE)

$$J(S,I,R,B)=\begin{bmatrix} \Lambda-(\mu h+\theta)S-(1-\Psi e)\lambda s & 0 & \phi R & 0 \\ (1-\Psi e)\lambda s & -(\mu h+d+\gamma\theta)I & 0 & (1-\psi e)\in I \\ 0 & \gamma I & -(\mu h+\phi)R & 0 \\ 0 & 0 & b*(1-(\omega b/KB)B) & -(\mu p+\omega b)B \end{bmatrix}$$

5. Conclusion

The model allows for a more comprehensive understanding of how various interventions interact and contribute to controlling the spread of the disease. Implementing multiple control measures simultaneously leads to a synergistic effect, resulting in a steady increase in the recovered population over time. This indicates that the combination of vaccination, education campaigns, therapeutic treatment, and water sanitation is effective. These measures collectively contribute to reducing the spread of cholera and improving recovery rates among infected individuals. The linear progression suggests that the effectiveness of the control measures is consistent throughout the simulation period. This sustained impact is crucial for managing cholera outbreaks and preventing further transmission.

6. Recommendations

Below are the recommendations from the study:

1. Implement Comprehensive Sanitation Measures by enhancing the sanitation infrastructure to reduce the transmission of Vibrio cholerae through contaminated water sources, addressing the root cause of cholera outbreaks
2. Prioritize Vaccination Campaigns by focusing on vaccinating susceptible individuals to lower the rate of infection and create a protective barrier against cholera outbreaks
3. Utilize computational power and data availability to predict the timing and magnitude of cholera outbreaks, incorporating real-time data on factors like weather, water quality, and sanitation.
4. Optimize control strategies by simulating different combinations of interventions within the model framework, identifying the most effective and cost-efficient approaches for specific contexts.

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