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MODELING AND ANALYSIS OF THE SPREAD OF CHOLERA DISEASE IN NIGERIA WITH ENVIRONMENTAL CONTROLS

FATIMA SULAYMAN

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By

FATIMA SULAYMAN

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Master of Science

November, 2014

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DEDICATIONS

To God The Almighty Allah

My Husband: Abubakar Abdulkadir

My Parents: Sulayman Yanma Muhammad and Maimuna Abubakar

My Daughter: Rabiat Abubakar.

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Master of Science

MODELING AND ANALYSIS OF THE SPREAD OF CHOLERA DISEASE IN NIGERIA WITH ENVIRONMENTAL CONTROLS

By

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November, 2014

Chair: Isthrinayagy Krishnarajah, PhD

Faculty: Science

Cholera, a major public health problem in many developing countries in which Nigeria is not an exception. The control of deadly outbreaks remains a challenge. The main goal of this thesis is to develop and analyze a mathematical model for the control of cholera in Nigeria with vital dynamics, water hygiene, environmental sanitation and treatment as control strategies in curtailing the disease.

The effective basic reproduction number R_C that is used to control the transmission of the disease is obtained. The equilibrium points of the cholera model are determined. The disease-free equilibrium point is locally and globally asymptotically stable when the effective reproduction number, $R_C \leq 1$ where the disease always dies out. The endemic equilibrium exist for $R_C > 1$.

Bifurcation analysis for endemic equilibrium is also carried out using center manifold theory. Graphical representation of the evolution of the disease at various settings is shown for different control strategies. The model studied shows that with proper combination of control measures and rigorous effort cholera epidemic could be eradicated from our society. Numerical simulation is carried out using parameter values based on Nigeria demographic data to investigate the effect of control strategies on infected population.

Simulation of the model is carried out in two categories where first we simulate the model to know the effects of each parameter at low, moderate and high level on the infected population and the results shows that treatment play a vital role in controlling the cholera infection. While in second category, we simulate the model

with no control, low without treatment and low universal, moderate without treatment and moderate universal and lastly high without treatment and high universal.

Our results show that universal strategies is an effective method for controlling cholera. In fact, model studied shows clearly that improvement in treatment, water hygiene and the environmental sanitation offered to about fifty percent is all that is required to eradicate the diseases.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains

PEMODELAN DAN ANALISIS BAGI PENYEBARAN TAUN DI NIGERIA PENGAN KAWALAN PERSEKITARAN

Oleh

SULAYMAN FATIMA

Novumber, 2014

Pengerusi: Isthrinayagy Krishnarajah, PhD

Fakulti: Sains

Wabak taun merupakan salah satu masalah kesihatan utama di kalangan negara membangun, termasuk Nigeria. Kegagalan mengawal wabak tersebut mampu meragut nyawa dan mengawalnya merupakan satu cabaran besar. Tujuan utama tesis ini ialah untuk menyelidik dan menganalisa model matematik baru yang bertujuan untuk mengawal taun di Nigeria.

Model tersebut merangkumi dinamik tertentu iaitu, kebersihan air, kebersihan persekitaran dan perawatan. Penglibatan dinamik tersebut ialah strategi dalam usaha untuk mengawal taun. Berdasarkan model tersebut, nomber keberkesan pembiakan R_C, yang digunakan untuk mengawal penyebaran penyakit diperolehi. Di samping itu, titik-titik keseimbangan juga dikenalpasti.

Titik-titik keseimbangan (titik bebas penyakit) dinyatakan sebagai stabil secara asimtotik setempat dan sejagat apabila $R_C < 1$, dimana penyakit berkenaan dibasmi sepenuhnya. Analisis bifurkasi yang melibatkan keseimbangan endemik juga dilasanakan dengan menggunakan teori manifold tengo. Sehubungan itu, graf disertakan sebagai menyokong keputusan analitikal tersebut.

Model ini menunjukkan bahawa kesesuaian gabungan ukuran dan usaha gigih berpotensi untuk membasmi taun. Simulasi berangka dijalankan menggunakan data demografi Nigeria, untuk, mengkaji kesan strategi pengawalan populasi yang dijangkiti.

Simulasi berangka dijalankan terhadap kes tanpa kawalan, kes rendah tanpa rawatan dan rendah sejagat, kes sederhana tanpa rawatan dan sederhana sejagat, dan kes tinggi tanpa rawatan dan tinggi sejagat. Hasil kajian menunjukkan bahawa strategi

sejagat adalah cara berkesan mengawal wabak berkenaan. Model ini juga menunjukkan dengan jelas peningkatan dalam perawatan air dan kebersihan persekitaran di sekitar lima puluh peratus cukup untuk membasmi taun di Nigeria.

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I certify that a Thesis Examination Committee has met on 28 November 2014 to conduct the final examination of Fatima Sulayman on her thesis entitled "Modeling and Analysis of the Spread of Cholera Disease in Nigeria with Environmental Controls" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Master of Science.

Members of the Thesis Examination Committee were as follows:

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Professor
Faculty of Science
Universiti Putra Malaysia
(Chairman)

Mohd Rizam b Abu Bakar, PhD
Associate Professor
Faculty of Science
Universiti Putra Malaysia
(Internal Examiner)

Leong Wah June, PhD
Associate Professor
Faculty of Science
Universiti Putra Malaysia
(Internal Examiner)

Mustafa bin Mamat, PhD
Professor
The Graduate School
Universiti Sultan Zainal Abidin
(External Examiner)

ZULKARNAIN ZAINAL, PhD
Professor and Deputy Dean
School of Graduate Studies
Universiti Putra Malaysia

Date: 23 January 2015

This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of **Master of Science**.

The members of the Supervisory Committee were as follows:

Isthrinayagy Krishnarajah, PhD
Senior Lecturer
Faculty of science
Universiti Putra Malaysia
(Chairperson)

Mohd Bakri Adam, PhD
Senior Lecturer
Faculty of Science
Universiti Putra Malaysia
(Member)

BUJANG BIN KIM HUAT, PhD
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LIST OF ABBREVIATIONS

ODEs	Ordinary Differential Equations
CDC	Center For Disease Control
WHO	World Health Organization
V.Cholerea	Vibrios Cholerea
UNICEF	United Nations Childrens Fund
CIA	Central Intelligence Agency
ORT	Oral Rehydration Therapy
DFE	Disease Free Equilibrium
EE	Endemic Equilibrium
R_0	Basic Reproduction Numbers
R_C	Effective Basic Reproduction Numbers
CFR	Case Fatality Rate

CHAPTER 1

INTRODUCTION

Cholera is an infectious intestinal disease that is caused by a bacterium known as Vibrio cholerae (Colwell, 1996; Hartley et al., 2005). Despite of a hundred years studies on the disease, according to statistics obtainable at WHO, it is estimated that there is 3-5 million cholera cases and 100, 000-120,000 deaths due to cholera each year. Environmental conditions and war do play major roles in spreading the disease in communities: this makes it a threat to the world. Also, "the short incubation period of two to five days potentially enhance the explosive pattern of outbreaks" WHO (2013). As such, understanding the dynamics of the disease is quite important.

Cholera transmission is present in places where there is environmental mismanagement. New outbreaks can occur regularly around poor areas where food safety, sanitation, clean water and hygiene are not available. The greatest risk occurs in overcrowded communities and refugees by unsafe drinking and poor sanitation. WHO (2013) records showed that the transmission of bacteria are via contaminated food or drinking water. "Cholera remains a global threat to public health and a key indicator is of lack of social development. In the modern times, the recurrence of cholera has been noted in parallel with the ever-increasing size of vulnerable populations living in unsanitary conditions. For 2011 alone, a total of 589 854 cases were notified from 58 countries, including 7816 mortals. Many more cases were unaccounted for due to limitations in surveillance and fear of trade travel sanctions."

"Cholera epidemic is naturally volatile in nature, once introduced into the populations that is lacking prior immunity to the organism and its spread through the population is fast and contains all age groups" (Hartley et al., 2005).

Despite constant efforts to limit the spread of cholera disease, it continues to cause epidemic and pandemic infection. The previous few years have experienced many cholera outbreaks in developing countries, which includes, among others, those in India (2007), Congo (2008), Vietnam (2009), Iraq (2008), Zimbabwe (2008-2009), Kenya (2010), Nigeria (2010) and Haiti (2010) as given in Tian and Wang (2011), leading to several million cases annually (Sack et al., 2006). Outbreaks interrupt social structures, encumber economic development and probably causes around 100,000 deaths almost a year (Longini Jr et al., 2007).

Ma and Ma (2006) state that in order to understand an efficient way to control (treat and prevent) an infection, it will be good to study its transmission behavior over a period of time. Mathematical model of epidemiology plays a significant role in understanding how to control and eradicate diseases.

According to Kaplan and Brandeau (1994) " Mathematical models are used extensively in the study of ecological and epidemiological phenomena. They are particularly helpful as experimental tools with which to evaluate and compare control procedures and preventive strategies, and to explore the relative effects of various biological, sociological and environmental factors on the spread of diseases."

1.1 Overview of Cholera

History

According to Cook (1996) "Some of the earliest recorded evidence of a cholera-like disease comes from the ancient Greek writings of Hippocrates around 470-400 B.C. and in the Sushrute Samhita, a Sanskrit text from around 500-400 B.C. Modern accounts of epidemics across Asia record outbreaks starting from 1438 and continuing to the present time. It was not until 1817 that the modern pandemics began, and cholera started to spread further abroad. The First Pandemic (1817-1823) began in Kishnagur, India in May of 1817. By the end of the pandemic, cholera had spread over 1000 in longitude, and 670 in latitude without reaching Europe. The second pandemic (1826-1837) spread from India, across Asia and Europe, and by 1834 had even reached most major cities in the United States and Canada. The third and fourth pandemics (1846-1863 and 1865-1875 respectively) spread much like the second Pandemic, though with more virulence. In 1854, during the third pandemic, 23,000 people were killed in England and Wales, and even more in southern Europe."

WHO (2013) report also showed that "during the 19th century, cholera spread across the world from its original reservoir in the Ganges delta in India. Six subsequent pandemics killed millions of people across all continents. The current (seventh) pandemic started in South Asia in 1961, and reached Africa in 1971 and the Americas in 1991. Cholera is now endemic in many countries. 45,159 cases and 3488 deaths in 10 African nations were reported up to 23 July 1991. Recently, the re-emergence of cholera has been noted in parallel with the ever-increasing size of vulnerable populations living in unsanitary conditions. From August 2008 to February 2009, more than 79,000 cases and 3,700 deaths were reported from a single country, Zimbabwe. Regardless of the advancement of medical science and health care service, cholera remains a global threat to public health and one of the key indicators of social development."

1.2 Transmission

According to Kirschner et al. (2008) outbreak of cholera is cause by two serogroups of V. cholera - 01 and - 0139. The majority of cholera outbreak are cause by V. cholera 01 , while -0139 was first discovered in Bangladash in 1992 is confined to South-East Asia. Non-01 and non-0139 V. cholera do not generate epidemics but can cause mild diarrhea. Vibrio cholerae is a bacterium gram–negative, in the

shape of stick curved, mobile, with a single polar flagellum.

"Pathogenic V. cholera can survive refrigeration and freezing in food supplies. The dosage of bacteria required to cause an infection in healthily volunteers via oral administration of living vibrios is greater than 1000 organisms" (Hartley et al., 2005). "After consuming an antacid, however, cholera development in most volunteers after consumption of only 100 cholera vibrios experiments also show that vibrios consumed with food are more likely to cause infection than those from water alone" (Finkelstein, 1996).

Most of the infections occurred in children ages between 1 to 5 years, as cases attend to be clustered by season as well as location. "Increased protection against the cholera disease can be gained by improving sanitation and hygiene. Most cases of cholera currently occur in developing countries. Cholera is currently endemic in India and Bangladesh near the Bay of Bengal as well as in coastal regions of South America" Faruque et al. (1998) .

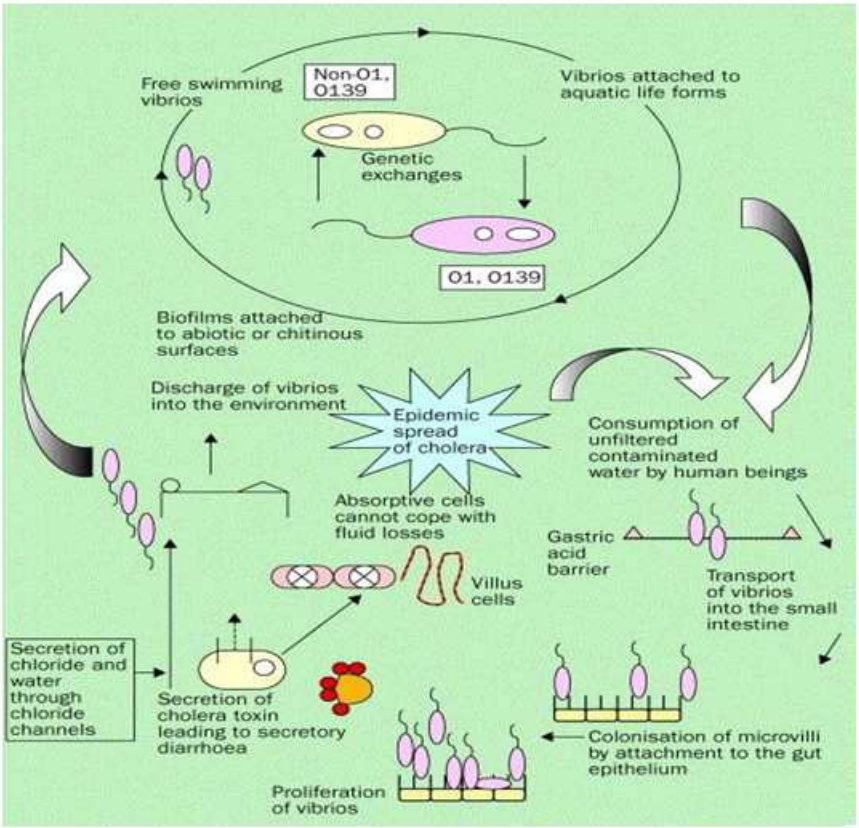

Figure 1.1: The life cycle of V.cholerae.
(Bayleyegn, 2009)

Figure 1.1 shows the life cycle of V.cholerae and is from (Bayleyegn, 2009).

1.3 Symptoms

The report by WHO (2013) describes cholera as " an extremely virulent disease. It affects both children and adults and can kill within hours. About 75% of people infected with V. cholerae do not develop any symptoms, although the bacteria are present in their faeces for 7-14 days after infection and are shed back into the environment, potentially infecting other people. Among people who develop symptoms, 80% have mild or moderate symptoms, while around 20% develop acute watery diarrhoea with severe dehydration. This can lead to death if untreated. People with low immunity such as malnourished children or people living with HIV are at a greater risk of death if infected. It has a short incubation period from less than one day to five days and produces an enterotoxin that causes watery diarrhea, copious and painless, that can quickly lead to severe dehydration. In the absence of treatment one can die in some few hours." Vomiting also occurs in most patients

Cholera infection results from absorption, by consumption, of the vibrio cholerae present in water or food, but also can be the result of a contaminated person to another person through pathological products (vomiting, saddles, sweat). Experiments show that the vibrios introduced into food have a higher chance of causing infection than those consumed in water. The infectious amount, in experiments given is of the order of 10^8 with 10^{11} bacteria (Cash et al., 1974).

1.4 Treatment and diagnosis

In order to treat cholera, the guidelines provided by WHO (2013) state thus: "cholera is an easily treatable disease. Up to 80% of people can be treated successfully through prompt administration of oral rehydration salts (WHO/UNICEF ORS standard sachet). Very severely dehydrated patients require administration of intravenous fluids. Such patients also require appropriate antibiotics to diminish the duration of diarrhoea, reduce the volume of rehydration fluids needed, and shorten the duration of V. cholerae excretion. Mass administration of antibiotics is not recommended, as it has no effect on the spread of cholera and contributes to increasing antimicrobial resistance. In order to ensure timely access to treatment, cholera treatment centres (CTCs) should be set up among the affected populations. With proper treatment, the case fatality rate should remain below 1%."

1.5 Epidemiology of Cholera in Nigeria

Cholera is an underreported disease. In Nigeria, outbreaks of the cholera disease have been occurring with increasing frequency since the first outbreak in modern times in 1970 (Epstein, 1993; Lawoyin et al., 1999). The disease is endemic in Nigeria and the outbreaks are not unusual (Adagbada et al., 2012). The intensity of cholera outbreak in majority town has been attributed to improper sanitation, acute water supply and poor sewage disposal(Wilson, 1971; Fatiregun et al., 2012). More so, constant power supply have affected the availability of pipe–borne water

which to large extent exposes communities to consumption of untreated water. The views expressed above can be corroborated with the report of WHO (2012) which highlight the first cholera outbreak in Nigeria in 1970. The epidemic which occurred in a village near Lagos recorded 22,931 cases and 2945 deaths of which a case fatality rate (CFR) of 12.8%.

However, the dynamic nature of cholera–like disease have made reports on cholera outbreak in Nigeria to be inconsistent. Nonetheless, three major epidemics have been recorded in the last two decades. These epidemics occurred in 1992, 1995-1996, and 1997 (Umoh et al. (1983); Hutin et al. (2003); and Usman et al. (2004);Hutin et al. (2003)). "Epidemiological records from Public Health Department of Kano State Ministry of Health, Northern Nigeria, discovered that the regularity and distribution of recurrent cholera epidemics in the state during 1995 to 2001, were 2 630 in 1995/1996, 847 in 1997 and 2, 347 in 1999" (Usman et al., 2004). In Jos, North Central Nigeria, Opajobi et al. (2004) "observed that all inaccessible strains were Vibrio cholerae 01 Eltor of Inaba serotype. The authors concluded that Vibrio cholerae 01 is endemic in Jos, Nigeria." Still in Northern Nigeria, an outbreak of gastroenteritis related to V. cholera serotype "Ogawa" affected some communities Katsina State around 1982 with CFR of 7.7% (Umoh et al., 1983). In Southern part of Nigeria, specifically in Calabar the outbreak affected mostly the adults and those within age bracket of 11-20 regardless of sex (Umoh et al., 1983).

Similarly result was reported by Opajobi et al. (2004) on Jos (North-central) with maximum isolation rate to be between age group 20-29 years. Hutin et al. (2003) said that "the 1996 epidemic reported in Kano, Northern Nigeria affected 1,384 individuals with a fatality rate of 5.3%." "Children were the most affected among all age groups and reported for 22% of the total cases accounted in Ibadan, south-west Nigeria" (Lawoyin et al., 1999).
Sow et al. (2011) "The wave of the El Tor cholera pandemic that took place in 1991 had a case fatality ratio of 13% in Nigeria ."

In Abeokuta, South-western Nigeria, between November 2005 and January 2006, 11 deaths from 115 cases with case fatality rate of 9.6 % was reported from a cholera outbreak (Shittu et al., 2010). Authors have argued that cholera exist as a seasonal disease although the degree of occurrence is more during rainy seasons. Pascual et al. (2002) highlighted the importance rainfall as a major influencer of seasonal cycle of cholera. This is likely through fast transmission waterborne diseases. In line with this, Umoh et al. (1983) contend that higher numbers of cases was observed in Kano during the raining season. In contrast, Ndon et al. (1992) said that the incidence of cholera outbreak mostly occurred during the dry season in South–Southern (Calabar) of the country. This is usually followed by subsidence at the beginning of rainy season. However, "seasonality of infection is not a critical issue in Nigeria as infections have been reported in both rainy and dry seasons" (Adagbada et al., 2012).

In summary United Nation (UN) unit, reports: "despite Nigeria's oil wealth, more than 70% of the country's 126 million people live below the poverty line and cholera outbreaks are common in poor urban areas which lack clean drinking water and proper sanitation" (UN, 2005). Obviously, it has been clear that cholera transmission is endemic in Nigeria. Hence this research study provides a mathematical insight of the effect of treatment, water hygiene and environmental sanitation in the dynamics of cholera diseases.

1.6 Mathematical Modelling

Mathematical modelling is defined by Benyah (2008) as the "process of creating a mathematical representation of some phenomenon in order to gain a better understanding of that phenomenon." It has become a very important scientific technique over the past 20 years. "Mathematical models offer an important tool to capture a set of assumptions and to follow them to their accurate logical conclusions." Essentially, any real situation in the physical and biological world, whether natural or involving technology and human intervention, is subject to analysis by modelling if it can be described in quantitative terms. Thus, optimization and control theory may be used to model industrial processes, traffic patterns, sediment transport in streams, and other situations; information and communication theory may be used to model message transmission, linguistic characteristics, and the like; and dimensional analysis and computer simulation may be used to model atmospheric circulation patterns, stress distribution in engineering structures, the growth and development of landform, and a host of other processes in science and engineering. "Once a model has been developed and used to answer questions, it should be seriously examined and often modified to obtain a more accurate reflection of the observed reality of that phenomenon." Benyah (2008) supports that mathematical modelling is an evolving process, as new insight is achieved, the process starts all over again as additional factors are considered.

1.7 Problem Statement

Cholera is the most feared of all diarrheal in the world, especially in developing countries (Seas and Gotuzzo, 1996). Few infectious diseases can influence the economy of developing countries in a negative way as cholera does. The disease is endemic in Nigeria and claims many lives. It has been noted that high transmission rate of the diseases is as a result of contaminated food and water. In developed world, seafood is the usual cause while in developing countries like Nigeria it is more often water. Despite the several interventions currently in place, the absence of effective proper sanitation improvement as the main intervention leading to safeguarding food security in the previous studies is the main problem. It is therefore the objective of this research study to formulate and analyze a mathematical model that incorporates vital dynamics, treatment, water hygiene and environmental sanitation. Hence, this research work is motivated by the fact that

although cholera epidemic is one of the most infectious diseases, not much research has been done in the area of its epidemiological modelling in Nigeria.

1.8 Significance of Study

Cholera is a threat to world public health, indicating a lack of social development. It is particularly endemic in Nigeria. However, in the case of Nigeria, there is no any mathematical model that has been developed on the dynamics of cholera transmission with special emphasis on the effects of water hygiene, environmental sanitation and treatment, so far, to the best of our knowledge. Therefore, the study will be significant to the society in the following ways:

1. The results on the effects of treatment, water hygiene and environmental sanitation in cholera dynamics would be necessary in raising awareness among decision makers to ensure that the national health network is prepared and equipped in order to prevent, minimize or eradicate cholera.
2. The result of this research work can be used as a guide for policy makers on long term social and economic effects of cholera in Nigeria.
3. This study will structure a support for further mathematical studies on cholera in Nigeria..

1.9 Research Objectives

The objective of this research work is categorized into general and specific objectives respectively.

1.9.1 General Objective

The most important goal of this study is to develop and analyze a mathematical model that shows the dynamics of cholera transmission in Nigeria and also come up with control measures to make possible for the decrease of the transmission of the disease in the country.

1.9.2 Specific Objective

This research work has the following specific objectives:

1. To formulate mathematical model of cholera transmission and control based on a compartmental SIRS model by incorporating vital dynamics, treatment, environmental sanitation and water hygienic practice.
2. To determine the effect of control measures on the infected population.
3. To obtain the disease-free and endemic equilibrium state points of the model for Nigeria.

4. To find the effective basic reproduction number R_C, of the model,

5. Obtain numerical simulation of the model using parameter values based on Nigerian demographic data.

1.10 Thesis Organization

This thesis consists of seven main chapters, chapter one provides background of cholera transmission, problem statement, aims and objectives as well as significance of the study. In chapter two we reviewed some literatures in the mathematical modelling of cholera. Chapter three provides some of the basic mathematical techniques needed to qualitatively analyze the model in this thesis. The chapter provides an introduction into the equilibria and stability theory, their general categories and application areas. The chapter also briefly discusses some of the principles and methods associated with disease modelling. Chapter four present the methodology used in carrying out the study. In chapter five numerical simulation of the model is carried out using single strategy. In chapter six numerical simulation of the model is carried out using combined strategies and finally, the research findings, conclusions and recommendations of the thesis are discussed in chapter seven.

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