A MATHEMATICAL MODEL FOR MALARIA

A CASES STUDY SOME SELCETED HEALTH CENTERS IN JINJA DISTRICT OF UGANDA

BY

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A RESEARCH REPORT SUBMITTED TO THE FACULTY OF EDUCATION, OPEN AND DISTANCE E- LEARNING IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF A BACHELOR OF SCIENCE WITH EDUCATION OF KAMPALA INTERNATIONAL UNIVERSITY

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DECLARATION

I Wakainja Abunel declare that this research report is my original work. It has not been submitted to any other University or higher institution for any award.

Signature ..... Date..04/10/2018

APPROVAL

I hereby certify that this work entitled A Mathematical Model for Malaria Transmission Dynamics in Jinja District of Uganda has been submitted with the approval of my university supervisor.

Signature ..... Date: 04-10-2018

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SUPERVISOR

DEDICATION

To my beloved parents Mr. Mafuko john and Ms. Kasuubo Elizabeth Mutibwa and my friends Abuo Bernadette , Ngobi Derik, and my Brother Byansi James for their financial support towards my education. May the lord bless you

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I thank the lord almighty for keeping, protecting and giving me sound mind and endurance during the course of my study.

I would like to appreciate the work of my supervisor Dr. Onuorah Martins who diligently guided me during my research. May the Almighty reward him abundantly.

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I would like to appreciate my beloved brother and sister; for their encouraging company and support. It is key for my success. My friends for their incredible contribution towards my education

I also wish to thank my lecturers for their advice, knowledge and guidance towards my education. May the good God bless them

Finally I take this opportunity to acknowledge the efforts of my respondents who availed all the necessary data during this research study

ABSTRACT

In this research work, a deterministic mathematical mode for malaria transmission was developed and analysed. The model consists of seven ordinary differential equations with two sub-populations. The human subpopulation consists of the susceptible, exposed, infected human compartments while the mosquito sub-population consists of the susceptible, exposed and infected mosquito compartments. The disease free and endemic equilibrium were obtained and analysed for stability. Further, the basic reproductive number of the model was obtained.

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CHAPTER ONE

1.0 The Introduction.

This chapter expounds on the background of the study, statement of the problem, objectives of the study, significance and scope of the study.

1.1 Background of the study

Malaria is a life threatening disease; it's typically transmitted through the bite of an infected Anopheles mosquito. Infected mosquitoes carry the plasmodium parasite that is released into the blood stream.

Malaria is one of the leading causes of death in the developing countries today, while prevention and treatment methods are available, their large sealer usage is a major drain on government budgets and not applied whenever necessary

Malaria is one of the major causes of mortality and mobility, with unknown number of 1-2.7 million patients dying annually and hundreds of millions afflicted the need for containment and for reduction of the health burden is obvious. But due to the scarcity of resources and lack of clear policy of their distribution, this control not attained. Even though theatiology of the disease has been known for a century, the full application of this knowledge requires a practical model for a decision making process .This model must be either robust enough to reflect all conditions or preferably perhaps flexible enough to be adaptable to local conditions. The development of such a model, and the training of the model to local conditions which can be applied to the changing conditions, is a formidable task. Such a model must attempt to combine various sources of data regarding the different aspects the disease dynamics and link these aspects with external causes .the model should be developed in a way in which the new segments may be added into the modeling structure. Hence a modular structure is required, allowing for evaluation and adapting sub processes, which may be defined, measured and tested in the laboratory or field settings. Parameter values may be introduced empirically and may be amended to reflect changes due to trends or to human intervention

The principal malaria transmission models to date are a few general forms. There are statistical models which compare malaria transmission variables. In addition there are dynamic models relating relating malaria transmission to constant climate conditions.

The present report wishes to fill part of the niche with some basic groundwork towards a complete numerical model for the weather based epidemiology of falciparum malaria. the report will present a simple model of malaria transmission.

1.2 Problem statement

Despite the effort and progress made by the world health organization and the ministry of health in Jinja district to eradicate malaria, it has rebounding in Jinja district since 2005. The health sector reported an increasing number of malaria cases since May 2014. And the district requested for an assistance to control the spread of this infection. Malaria is a very dangerous infection on human health; it causes body fever, loss of appetite, death, and loss of manpower due to the illness. It also costly to treat in terms of the drugs as most vulnerable are poor. It is from these alarming effects that the researcher seeks to find outs the remedy of this infection. And to dispose its impacts in the selected health centers in Jinja district in eastern Uganda.

1.3 The purpose of the study

The purpose of this research study is to develop and analyze a mathematical model for the transmission dynamics of malaria in Jinja district Uganda.

1.4 Objectives of the study

The objectives of the study are as follows

1. To develop the mathematical model for the dynamic of the disease.
2. To obtain the equilibrium state of the model.
3. To analyze the equilibrium state for stability.
4. To obtain the basic reproductive number

1.5 Significance of the study

The study about the impacts and causes as well as the control measures of malaria infection is very relevant to various groups and individuals not only in Uganda but in the world at large.

To begin with this study will help the national bureau of statistics to know the virology and medical background of malaria as necessary for national health evaluation specifically on this disease.

The study will assist the ministry of health in determining measures to solve and prevent the spread of malaria in the region.

The study will benefit students in Kampala International University, and the general public at large as it will add to existing work in their library on malaria disease. This research work will also have a significant role in the community toward awareness and public caution about the spread of the infections, the government therefore can rely on its findings to help the groups and individuals concerning this disease

1.6 Research questions

1. What are the causes and effects of malaria infection?
2. What is the mode and rate of transmission of malaria?
3. What are the symptoms of malaria infection?
4. What is the cure and prevent measures for malaria?

1.7 Scope of the study

1.7.1Contextual scope

Contextually, this research work is focus on investigating the impacts of malaria epidemics, its causes and symptoms plus its prevention measures in Jinja district.

1.7.2 Geographical scope

It has further been centralized on the population sample of Rippon hospital in Jinja District in eastern Uganda. It is located at approximately100km from Kampala

1.7.3 Time scope

This study was carried out in the period of six months that is from March 2018 to September 2018.

CHAPTER TWO

2.0 Virology and medical background

2.1.1 Virology

Malaria is an acute febrile illness with the clinical manifestation of the disease associated with the development of the asexual parasites in the blood.

The formation of hemozoin (malaria pigment) is a type of biomineralisation or biocrystallisation process that is initiated by oriented nucleation (Hempelmann et al., 2003; Egan et al., 2002). This nucleation process is induced by the 1-myristoyl-glycerol lipid molecules (MMG) through stereospecific interactions at the {100} crystal face (de Villiers et al., 2009).

The molecular units of the hemozoin crystal consist of ferricprotoporphyrin IX cyclic dimers. These dimers reciprocally link through coordination complexes between the carboxyl group of a propionate side chain of one molecule and the central iron atom of another (Fitch et al., 2003; Slater et al., 1991). The remaining free propionic acid groups of the dimers interact via intermolecular forces to form a hydrogen 8 bond network, with the head to tail dimers π-stacked along the [010] direction of the crystal face (Chong & Sullivan, 2003; de Villiers et al., 2009; Fitch, 2004).

Thereafter hemozoin construction takes place inside the digestive vacuole to assemble a membrane impenetrable crystal with 100 nm x 100 nm x 500 nm dimensions, containing over 10 000 000 haemes (Pisciotta& Sullivan, 2008). The crystal has two fast growing faces at the end of the β–haematin needle. This is due to the {001} crystal surface corrugation and O-H-O hydrogen bonds between the propionic acid groups of neighboring molecular units.

2.1.2 Medical back ground

Malaria stretches from its prehistoric origin as a zoonotic disease in the primates of Africa through to the 21st century. A widespread and potentially lethal human infectious disease, at its peak malaria infested every continent, except Antarctica. Its prevention and treatment have been targeted in science and medicine for hundreds of years. Since the discovery of the parasites which cause it, research attention has focused on their biology, as well as that of the mosquitoes which transmit the parasites.

For thousands of years, traditional herbal remedies have been used to treat malaria. The first effective treatment for malaria came from the bark of cinchona tree, which contains quinine. After the link to mosquitos and their parasites were identified in the early twentieth century, mosquito control measures such as widespread use of the insecticide DDT, swamp drainage, covering or oiling the surface of open water sources, indoor residual spraying and use of insecticide treated nets was initiated. Prophylactic quinine was prescribed in malaria endemic areas, and new therapeutic drugs, including chloroquine and artemisinins, were used to resist the scourge. Today, artemisinin is present in every remedy applied in treatment of malaria. After introducing artemisinin as a cure administered together with other remedies, the mortality in Africa went down by a half.

Malaria researchers have won multiple Nobel Prizes for their achievements, although the disease continues to afflict some 200 million patients each year, killing more than 600,000. Malaria was the most important health hazard encountered by U.S. troops in the South Pacific during World War II, where about 500,000 men were infected. According to Joseph Patrick Byrne, "Sixty thousand American soldiers died of malaria during the African and South Pacific campaigns."

At the close of the 20th century, malaria remained endemic in more than 100 countries throughout the tropical and subtropical zones, including large areas of Central and South America, Hispaniola (Haiti and the Dominican Republic), Africa, the Middle East, the Indian subcontinent, Southeast Asia, and Oceania. Resistance of Plasmodium to anti-malaria drugs, as well as resistance of mosquitoes to insecticides and the discovery of zoonotic species of the parasite have complicated control measures.

2.2 Transmission, signs and symptoms

2.2.1 Transmission

Malaria infecting humans is caused by four species of single Plasmodium with Plasmodium falciparum other species are Plasmodium vivax cycle of Plasmodium falciparum extra-cellular environments and to evade its hosts' immune responses (Florence 2002). The life cycle is divided into sexual stages in the mosquito and asexual stages in the human host.

The disease can be spread to people livening around swampy areas which are breeding places for mosquitoes.

2.2.2Signs and symptoms of Malaria

Malaria is an acute febrile illness with the clinical manifestation of the disease associated with the development of the asexual parasites in the blood. The onset of pathology is triggered by the rupture of erythrocyte membranes that releases merozoites and erythrocyte material into the circulation (Clark & Schofield, 2000). The released parasite antigens, pigment and malarial toxins induce production of pro-inflammatory cytokines, tumour necrosis factor (TNFd), interleukin-1 (IL-1) and IL-6 that result in an immune response from the host (Gilles, 1997; Miller et al., 1994). Thus, the first signs and symptoms of malaria are fever followed by;

- Headache
- Chills and
- Vomiting.

These symptoms appear 10 - 15 days after an infectious mosquito bite. In uncomplicated malaria the first symptoms are non-specific and resemble those of influenza, which makes the diagnosis of the disease difficult. If the infection is not treated within 24 hours the uncomplicated case can progress to severe illness that often leads to death (WHO 2010). In untreated malaria the infected erythrocytes adhere to the vascular endothelium (cytoadherence) and disappear from circulation. This process is referred to as sequestration and compromises the microcirculation in vital organs. In addition to sequestration, the formation of erythrocyte clumps through rosetting, where uninfected erythrocytes adhere to infected erythrocytes, further compromise blood flow to vital organs (Dondorp; 2005). Cytoadherence, rosetting and autoagglutination lead to microcirculatory

obstruction in patients and result in reduced oxygen supply that causes anaerobic glycolysis, lactic acidosis and cellular dysfunction (White, 2002). Other complications of the disease include coma, renal failure, noncardiac pulmonary oedema, anaemia, liver dysfunction, gastrointestinal dysfunction, placental dysfunction, acidosis, hypoglycaemia and bacterial infections. Death in children suffering from severe cases of the disease is often attributed to cerebral malaria, malarial anaemia or metabolic acidosis (Gilles, 1997).

2.3 Diagnosis, treatment and prevention.

2.3.1 Diagnosis

The use of antigen-based malaria rapid diagnostic tests (RDTs) emerged in the 1980s. In the twenty-first century Giemsamicroscopy and RDTs became the two preferred diagnostic techniques. Malaria RDTs do not require special equipment and offer the potential to extend accurate malaria diagnosis to areas lacking microscopy services.

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hypoglycaemia and bacterial infections. Death in children suffering from severe cases of the disease is often attributed to cerebral malaria, malarial anaemia or metabolic acidosis

The symptoms of acute malaria are so distinctive that laboratory diagnosis is seldom required. However, as the vaccination program progresses, atypical forms of malaria have emerged and laboratory diagnosis may be required.

(i). Microscopy - production of multinucleate giant cells with inclusion bodies is pathognomonic for measles. During the prodrome phase, such cells are detectable in the NPS (nasopharyngeal secretions).

(ii). Immunofluorescence - direct and indirect immunofluorescence have been used extensively to demonstrate MV antigens in cells from NPS specimens. This technique can also be applied to the urine as such cells may be present in the urine 2 to 5 days after the appearance of the rash. (Although like mumps, measles virus is also excreted in the urine, this route is unlikely to play a significant role in the spread of the virus infection.)

2.3.2 Malaria treatment

The eradication campaign launched against malaria from 1940 to 1970 was the first attempt at global level to control the disease. The disillusionment that followed the emergence of monodrug- and multidrug resistance in Plasmodium falciparum, as well as Anopheles mosquito vector resistance to DDT spraying led to the abandonment of the global control efforts (Sachs, 2002). The recent increase in malaria incidence renewed the interest in innovative malaria research and new efforts to control rather than eradicate the disease. New initiatives for drug discovery, vaccine development and malaria research were launched in 1997 to 1999. These initiatives include Roll Back Malaria (RBM), the Medicines for Malaria 11 Venture (MMV), Multilateral Initiative on Malaria (MIM) and the Malaria Vaccine Initiative (MVI) (Sachs, 2002; Wellems, 2002).

The development of vaccines against malaria has made good progress with many potential candidates in clinical trials (WHO 2010). These include pre-erythrocytic vaccines that target sporozoites, asexual stage vaccines that target the merozoites, and a transmission blocking

vaccine against the sexual parasite stages in the mosquito vector (Breman et al., 2004). Although promising, there is currently no licensed vaccine available against malaria (WHO 2010). Therefore the mainstay of malaria treatment and prophylaxis still remain antimalarial chemotherapy. The antimalarial drugs possess selective actions on different stages of the parasite life cycle. These are:

• Blood schizonticides: antimalarial drugs that act on erythrocytic parasites by eliminating blood schizonts in the erythrocytes during the erythrocytic stage.

• Tissue schizonticides: drugs that prevent invasion of malaria parasites in erythrocytes by eliminating developing tissue schizonts or hypnozoites in the liver.

• Gametocides: drugs that destroy the sexual forms of the parasite in the blood and prevent transmission to mosquitoes.

• Sporontocides: antimalarial drugs that prevent the development of oocysts in the mosquito and render gametocytes non-infective (Katzung, 2001).

Antimalarial drugs

Many of the current antimalarial drugs can be divided into the broad groups of antifolates, artemisinins, quinolines and arylaminoalcohols. These groups are divided according to different pharmacophores, mechanism of action and selective action on different stages of the parasite life cycle.

The antifolate drugs

Humans and parasites have the ability to convert folic acid into tetrahydrofolic acid. While humans obtain the needed folic acid from their diet, the parasite has to synthesise its own dihydrofolic acid from dihydropteroic acid. This feature is responsible for the selective toxicity of antifolateantimalarials, which interfere with the parasite's folic acid synthesis (Vangapandu et al., 2006).

antifolates: sulphonamides and sulphones Sulphonamides such as sulphadoxine 1, and the sulphones such as dapsone 2, mimic paminobenzoic acid (PABA) and interfere with folic acid synthesis by preventing the formation of dihydropteroate. These compounds compete with the

parasitic enzyme dihydropteroate synthase (DHPS) for its active binding site (Olliaro, 2001). The drugs mainly act as blood schizonticides and are usually administered with pyrimethamine or other various combinations (Sweetman, 2009).

Atovaquone The combination of the hydroxynaphthoquinoneatovaquone and proguanil has a synergistic antimalarial activity effective for treatment and prophylaxis of malaria (Katzung, 2001). Atovaquone exhibits weak antimalarial activity when administered as an individual agent by acting as a blood schizontocide. The drug inhibits the parasite's cellular respiration by interfering with parasite mitochondrial electron transport and also depolarizing the parasite mitochondria (Strivastava& Vaidya, 1999; White, 2002).

2.3.3 Prevention

Insecticides

Efforts to control the spread of malaria suffered a major setback discovered imported disease-bearing *Anopheles gambiae* mosquitoes living (DNA analysis later revealed the actual species to be *A. arabiensis*). This species of mosquito is a particularly efficient vector for malaria. In the introduction of this vector caused the greatest epidemic of malaria.

DDT (**D**ichloro**D**iphenyl**T**richloroethane)

DDT is effective for six to eight weeks if sprayed on the inside walls and ceilings of houses and other buildings. Laboratory tests demonstrated that it was highly effective against many insects. The unprecedented effectiveness of the chemical was confirmed: the new insecticide was able to eradicate malaria by eradicating mosquitoes.

World Health Organization (WHO) launched an antimalarial program as a pilot project to determine the feasibility of malaria eradication in tropical Africa. However, these projects encountered difficulties that foreshadowed the general retreat from malaria eradication efforts across tropical Africa.

Pyrethrum

Other insecticides are available for mosquito control, as well as physical measures, such as draining the wetland breeding grounds and the provision of better sanitation. Pyrethrum (from the flowering plant *Chrysanthemum* is an economically important source of natural insecticide. Pyrethrins attack the nervous systems of all insects. A few minutes after application, the insect cannot move or fly, while female mosquitoes are inhibited from biting. The use of pyrethrum in insecticide preparations dates to about 400 BCE. Pyrethrins are biodegradable and break down easily on exposure to light. The majority of the world's supply of pyrethrin and *Chrysanthemum cinerariaefolium* comes from Kenya.

2.4.0 Life cycle and pathogenosis

2.4.1 Malaria infection cycle

Malaria infecting humans is caused by four species of single Plasmodium with Plasmodium falciparum other species are Plasmodium vivax cycle of Plasmodium falciparum extra-cellular environments and to evade its hosts' immune responses (Florence 2002). The life cycle is divided into sexual stages in the mosquito and asexual stages in the human host.

The pre-erythrocytic development and asexual blood-stage of the parasite life-cycle take place inside the human host. Transmission occurs with intravenous inoculation of malaria sporozoites into the bloodstream during a female mosquito bite. The sporozoites invade the hepatocytes within 45 minutes of inoculation and multiply in the liver, undergoing asexual schizogony. The schizont then ruptures to release thousands of merozoites into the bloodstream that invade erythrocytes and commence the erythrocytic cycle (Miller et al., 1994). Within 30 - 60 seconds the released merozoites penetrate the host's erythrocytes and transform into characteristic ring stage parasites. The immature trophozoites (ring stage) then mature to trophozoites (trophozoite stage). During this stage the parasite prepares the surface of the erythrocyte to mediate cytoadherence and ingests the erythrocyte's cytoplasmic contents, especially haemoglobin. The trophozoites develop into schizonts that undergo nuclear division followed by merozoite formation (Florence et al., 2002). The erythrocyte membrane ruptures to release between 6 - 36 merozoites back into circulation that rapidly re-invade other erythrocytes to continue asexual amplification (White, 2002). Approximately 1% of formed merozoites inside erythrocytes

differentiate into sexual forms of male micro-gametocytes and female macro-gametocytes which transmit the infection to the Anopheles mosquito (Oh & Chishti, 2005).

Plasmodium falciparum life cycle in the mosquito

The female Anopheles mosquito is the vector of malaria transmission to the human host. The mosquito stage in the parasite life cycle involves the sexual stages in its development and takes between 8 - 35 days. The cycle starts with the ingestion of a blood meal, and requires only one male microgamete and one female macrogamete for infection to occur (White, 2002). The ingested male and female gametocytes undergo gametogenesis in the mosquito's midgut to form a zygote. Within 24 hours the zygote differentiates into an ookinete, which penetrates the wall of the mosquito midgut and develops into an oocyst. The oocyst produces sporozoites that migrate to the salivary glands of the mosquito to invade the gland epithelium. In order for the life cycle to repeat itself, the sporozoites need to be inoculated into a human host during a mosquito blood meal (Oh & Chishti, 2005).

2.4.2 Pathogenesis

During the intra-erythrocytic stage the parasite ingests 75% of its human host's red blood cell content (RBC) (Buller et al., 2002). Haemoglobin is ingested from infected erythrocytes through a cytosome and transported in vesicles to the parasite's digestive food vacuole (Goldberg, 2005). Inside the digestive vacuole the haemoglobin is degraded by the parasite's proteases into globin chains and iron. These chains are enzymatically cleaved into small peptides needed as a source of amino acids for protein synthesis. The parasite uses the iron for nucleotide-, DNA-, pyrimidine- and haem synthesis and electron transport (Mabeza et al., 1999; Scholl et al., 2005). During this degradation process a noted byproduct (Fe2+) ferrous-protoporhyrin IX (free haem) is formed that can become toxic. This poses an exploitable problem for the parasite as it lacks haem oxygenase activity or iron storage proteins like ferritin (Scholl et al., 2005).

The parasite can only prevent the free haem from accumulating to toxic concentrations by incorporating it into hemozoin. To do this the (Fe2+) ferrous-protoporhyrin IX undergoes one electron oxidation to produce (Fe3+) ferricprotoporphyrin IX (haematin).

The haematin rapidly precipitates and forms inert cyclic dimers that crystallize under acidic conditions to form hemozoin (Buller et al., 2002; Fitch et al., 2003; Egan, 2008). This biocrystallisation process is of critical importance to the parasite in order to prevent oxygen radical production, which ideally takes place in the oxygen-rich and acidic environment of the digestive vacuole. In the event of hemozoin formation prevention the molecular oxygen readily accepts the iron electron to initiate a chain of oxygen radical metabolism through the Fenton reaction (O2 - + H2O2 ↔ HO + O2 + HO-), which produces damaging free radicals (Pisciotta& Sullivan, 2008; Sullivan, 2002).

If the biocrystallisation process is delayed or inhibited, the reactive oxygen species produced may induce oxidative stress, resulting in parasite death through a cascade of lethal events. These toxic effects include parasite DNA damage, inhibition of proteolytic enzymes, haemoglobin accumulation, ferri-protoporphyrin accumulation, lipid peroxidation of parasite membranes and parasite membrane impairment (Rayenes, 1999; Kumar et al., 2007).

2.5 Review of literature

The malaria parasites Malaria infecting humans is caused by four species of single-celled parasites of the genus Plasmodium falciparum being responsible for most human deaths. The Plasmodium vivax, Plasmodium malariae and Plasmodium ovale Plasmodium falciparum is adapted and specialized to survive different intra cellular environments and to evade its hosts' immune responses (Florence 2002). The life cycle is divided into sexual stages in the mosquito and asexual stages in the Plasmodium falciparum life cycle reproduced with permission 4 celled parasites of the genus responsible for most human deaths. The Plasmodium ovale. The life is adapted and specialized to survive different intra- and cellular environments and to evade its hosts' immune responses (Florence et al., 2002). The life cycle is divided into sexual stages in the mosquito and asexual stages in the reproduced with permission.

CHAPTER THREE

RESEARCH METHODOLOGY

3.0 Introduction

This section of the study indicates how the research is going to be carried out. It shows the research design, type of data and sources of data, the model formulation, Schematic diagram, Parameters of the model.

3.1.1 Research Design

This study used descriptive survey research design. According to Jackson (2009) descriptive research is used to obtain information concerning the current status of the phenomenon to describe „what exists with respect to variables or conditions in a situation.

The focus of the study is to model the dynamics of malaria in Jinja district using data from the selected health centers. Qualitative data will be collected from different medical personals via interviews, while quantitative data will be collected from staff members of the selected health centers in Jinja district.

3.2 Mathematical model of infectious diseases

The Modelling of infectious diseases is a tool which has been used to study the mechanisms by which diseases spread, to predict the future course of an outbreak and to evaluate strategies to control an epidemic (Daley and Gani, 2005).

The first scientist who systematically tried to quantify causes of death was (Graunt, 1662). The bills he studied were listings of numbers and causes of deaths published weekly. Graunt's analysis of causes of death is considered the beginning of the "theory of competing risks" which according to (Daley and Gani, 2005) is "a theory that is now well established among modern epidemiologists".

The earliest account of mathematical modelling of spread of disease was carried out in 1766 by Daniel Bernoulli. Trained as a physician, Bernoulli created a mathematical model to defend the practice of inoculating against smallpox (Hethcote, 2000). The calculations from this model showed that universal inoculation against smallpox would increase the life expectancy from 26 years 7 months to 29 years 9 months (Bernoulli and Blower, 2004).

Daniel Bernoulli's work preceded our modern understanding of germ theory, it was followed by (Hamer, 1906) model on malaria but it was not until the research of (Ross, 1911) into the spread of malaria, that modern theoretical epidemiology began. This was soon followed by the work of (McKendrick and Kermack, 1927) whose paper a Contribution to the Mathematical Theory of Epidemics was published in 1927. A simple deterministic (compartmental) model was formulated in this paper. The model was successful in predicting the behavior of outbreaks very similar to that observed in many recorded epidemics (Brauer and Castillo-Chavez, 2001).

3.2 Model formulation and analysis

In this section a deterministic, compartmental mathematical model to describe the transmission dynamics of malaria is formulated. It is assumed that the population is homogeneously mixing and reflects increasing dynamics such as birth and immigration, individual can be infected through falling to sleep under mosiqutoe net and areas fall of mosquitoes spreading malaria.

The total population (N) is divided into the following epidemiological classes: Susceptible, S (Individuals who may get the disease); Exposed or Latent, E (Individuals who are exposed to the disease); Infected, I (Individuals who have the disease); Recovered, R (Individuals who have infection-acquired immunity) If there is an adequate contact of a Susceptible individual with an Infective individual then transmission may occur, thus the susceptible individuals may join the Exposed class, E at the rate α. When Latent period ends, exposed individuals may progress to the Infectious class, I at rate σ. After some treatment, infectious individuals may recover and join

the recovery class, R at rate γ. Since the disease is fatal, infected individuals may die due to the disease at the rate δ or die naturally at rate μ. The mosquito population is divided into infected mosquito, exposed and susceptible.

Figure1. Schematic diagram of malaria transmission dynamics

The model equation

Deterministic mathematical model with relapse and loss of immunity.

$$\frac{dS_H}{dt} = \beta_1 + (1-\gamma)I_H + \rho R_H - \frac{\alpha_1 S_H I_m}{N_H} - \mu_1 S_H (1)$$

$$\frac{dE_H}{dt} = \frac{\alpha_1 S_H I_m}{N_H} - (\sigma_1 + \mu_1)E_H (2)$$

$$\frac{dI_H}{dt} = \sigma_1 E_H - (\gamma + \mu_1)I_H (3)$$

$$\frac{dR_H}{dt} = \gamma I_H - (\gamma + \rho + \mu_1)R_H (4)$$

$$\frac{dS_m}{dt} = \beta_2 - \frac{\alpha_2 S_m I_H}{N_H} - \mu_2 S_m (5)$$

$$\frac{dE_m}{dt} = \frac{\alpha_2 S_m I_H}{N_H} - (\mu_2 + \delta_2)E_m (6)$$

$$\frac{dI_m}{dt} = \delta_2 E_m - \mu_2 I_m (7)$$

Where.

$S_H(t)$ susceptible human population at time t

$E_H(t)$ exposed human population at time t

$I_H(t)$ infected human population at time t

$R_H(t)$ recovered human population at time t

$S_m(t)$ exposed human population at time t

$E_m(t)$ exposed human population at time t

$I_m(t)$ infected human population at time t

β_1 The birth rate of humanat time t

α_1 Infections rateof human at time t

γ Recovery rate of human at time t

μ_1 Death rate of human at time t

σ_1 progression rate from exposed to infectious

δ human death rate of human due to malaria

β_2 birth rate of mosquito recovery rate of human

α_2 infectious rate of mosquito

μ_2 natural death rate of mosquito death rate

σ_2 profussion from exposed to infectious mosquito stage

Type equation here.

CHAPTER FOUR

MODEL ANALYSIS

4.0 Data analysis

This chapter includes the model analysis of malaria in this study

4.1 Equilibrium state of the model

The model is built using ordinary differential equations in which the independent variable is expressed explicitly, called autonomous differential equation, i.e., equation of the form;

$$\frac{dx}{dt} = f(x), x \in R^n \tag{8}$$

in which the right hand side is independent of t, as opposed to non – autonomous system

$$\frac{dx}{dt} = f(x,t), x \in R^n \qquad t = [0,+\infty) \in R,\ f : R^n \times R \to R^n \tag{9}$$

where the function f can depend on the independent variable t.

The solutions of the equation $f(x) = 0$ are called the equilibrium points or steady state solution of the ordinary differential equation (ode) (6). It is the state of a system whose configuration or large scale properties do not change over time. For example, in mechanics a system is at equilibrium if the force acting on a body is equal to zero. If dynamic of a system is described by a system of differential equations, then the equilibrium can be estimated by setting the derivatives to zero.

Definition 4.1: A point $\bar{x} \in R^n$ is called an equilibrium point of the equation (6) if $f(\bar{x}) = 0$.

In epidemiology, the equilibrium can be zero, disease – free or endemic. At zero equilibrium, the population tends to extinction, the disease free – equilibrium is the state at which the population comprises of the susceptible and recovered individuals, while in the endemic equilibrium state each compartment of the sub population is greater than zero. It is important we emphasize here that in models with standard incidence and disease induced death we may not be able to explicitly find the coordinates of the equilibrium point, but we can at least show that it exists.

4.1.2 Disease Free Equilibrium (DFE)

There are three types of equilibrium states usually considered in epidemiological modelling; the zero equilibrium, the disease free equilibrium and the endemic equilibrium states. In this work, we consider the disease free equilibrium (DFE), and the endemic equilibrium states. Generally, at the equilibrium states, the rate of change of the state variables with respect to time is zero, i.e.

Let rates RHS $E_{H,}, I_{H,} E_{M,} I_{M=}0$

For DFE, i.e. equilibrium points where there is no disease, we define disease compartments as the exposed human, and Infected human compartments that is E and I respectively.

To obtain the DFE of the model, we set the right hand side of the model (1) to (7) to zero as given below;

$$\frac{dS_H}{dt} = \frac{dE_H}{dt} = \frac{dI_H}{dt} = \frac{dR_H}{dt} = \frac{dS_m}{dt} = \frac{dE_m}{dt} = \frac{dI_m}{dt} = 0$$

$$S_H = \frac{\beta_1 + \rho R_H}{\mu_1}$$

$$S_m = \frac{\beta_2}{\mu_2}$$

$$E_0 = (S_H, E_H, I_H, R_H, S_m, E_m, I_m) = \left[\frac{\beta_1 + \rho R_H}{\mu_1}, 0,0,0, \frac{\beta_2}{\mu_2}, 0,0\right] \quad (10)$$

4.2 Endemic equilibrium state

This is an equilibrium state where at least one of the infected compartments is non-zero. In order to find the Endemic equilibrium for our model equations (1) to (7), the following steps are taken.

We let

$$\lambda_1 = \frac{\alpha_1 I_m}{N_H}, \lambda_2 = \frac{\alpha_2 I_H}{N_H} \quad (11)$$

Substituting equation (11) into equations (1) to (7), we have

$$\frac{dS_H}{dt} = \beta_1 + (1-\gamma)I_H + \rho R_H - \lambda_1 S_H - \mu_1 S_H (12)$$

$$\frac{dE_H}{dt} = \lambda_1 S_H - (\sigma_1 + \mu_1)E_H (13)$$

$$\frac{dI_H}{dt} = \sigma_1 E_H - (\gamma + \mu_1)I_H (14)$$

$$\frac{dR_H}{dt} = \gamma I_H - (\gamma + \rho + \mu_1)R_H (15)$$

$$\frac{dS_m}{dt} = \beta_2 - \lambda_2 s_m - \mu_2 S_m (16)$$

$$\frac{dE_m}{dt} = \lambda_2 s_m - (\mu_2 + \delta_2)E_m (17)$$

$$\frac{dI_m}{dt} = \delta_2 E_m - \mu_2 I_m (18)$$

Solving equations (12) to (18)

$$\frac{dS_H}{dt} = \beta_1 + (1-\gamma)I_H + \rho R_H - \lambda_1 S_H - \mu_1 S_H$$

$$s_H(\lambda_{1+}\mu_1) = \beta_1 + (1-\gamma)I_H + \rho R_H$$

$$S_H^* = \frac{\beta_1 + (1-\gamma)I_H}{\lambda_{1+}\mu_1} (19)$$

$$\frac{dE_H}{dt} = \lambda_1 S_H - (\sigma_1 + \mu_1)E_H$$

$$(\sigma_1 + \mu_1)E_H = \lambda_1 S_H$$

$$E_H^* = \frac{\lambda_1 S_H}{\delta_1 + \mu_1} (20)$$

$$\frac{dI_H}{dt} = \sigma_1 E_H - (\gamma + \mu_1)I_H$$

$$(\gamma + \mu_1)I_H = \sigma_1 E_H$$

$$I_H^* = \frac{\sigma_1 E_H}{\gamma + \mu_1} (21)$$

$$\frac{dR_H}{dt} = \gamma I_H - (\gamma + \rho + \mu_1)R_H$$

$$(\gamma + \rho + \mu_1)R_H = \gamma I_H$$

$$R_H^* = \frac{\gamma I_H}{(\gamma+\rho+\mu_1)} (22)$$

$$\frac{dS_m}{dt} = \beta_2 - \lambda_2 s_m - \mu_2 S_m$$

$$S_M(\lambda_2 + \mu_2) = \beta_2$$

$$S_M^* = \frac{\beta_2}{\lambda_2+\mu_2} (23)$$

$$\frac{dE_m}{dt} = \lambda_2 s_m - (\mu_2 + \delta_2)E_m$$

$$(\mu_2 + \delta_2)E_m = \lambda_2 s_m$$

$$E_m^* = \frac{\lambda_2 s_m}{\mu_2+\delta_2} (24)$$

$$\frac{dI_m}{dt} = \delta_2 E_m - \mu_2 I_m$$

$$\mu_2 I_m = \delta_2 E_m$$

$$I_m^* = \frac{\delta_2 E_m}{\mu_2} (25)$$

4.3 The basic effective reproductive number

One of the most important concerns about any infectious disease is its ability to invade a population. Many epidemiological models have a disease free equilibrium (DFE) at which the population remains in the absence of the disease. The basic reproduction number, R_0 is a measure of the potential for disease spread in a population, and is inarguably 'one of the foremost and most valuable ideas that mathematical thinking has brought to epidemic theory' (Heesterbeek and Dietz, 1996). The basic reproductive number R_0 is the number of secondary infections that one infective individual would create over the duration of the infectious period when population is completely susceptible. On the other hand, the effective reproductive number R_c is the number of secondary infections that one infective individual would create over the duration of the infectious period when a portion of the population is protected. When $R_c < 1$, then the DFE is locally asymptotically stable, and the disease cannot invade the population, but if $R_c > 1$,then the DFE is unstable and invasion is always possible see Hethcote (1978).

Our model is suited for a heterogeneous population in which the vital and epidemiological parameter for an individual may depend on such factors as the stage of the disease, spatial position, etc. however, we assume that the population can be broken into homogeneous subpopulation or compartment such that individual in a given compartment are indistinguishable from one anoer.

We use the next generation matrix approach as described by Driessch and Watmough (2005) to derive our effective Reproductive Number R_c. Numerous other articles Dietz (1993), Heesterbeek (1992), Roberts (2003), Simon (1992), and Diekmann (1990), are devoted to the calculation of basic reproductive number R_0 for different models of various diseases.

Our model has two Infective compartments, namely the Infective (I) and Exposed. It follows that the matrices F and V for the new infective terms and remaining transfer terms respectively are given below. Where the entries of F and V are partial derivatives of $f_i(x)$ and $V_i(x)$. For our model, F and V are given below.

F V infectious classes (E, I)

$$F=\begin{pmatrix} 0 & 0 & 0 & \propto_1 \frac{S_H}{N_H} \\ 0 & 0 & 0 & 0 \\ 0 & \frac{\propto_2 S_M}{N_H} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

$$V=\begin{pmatrix} -(\delta_1+\mu_1) & 0 & 0 & 0 \\ \sigma_1 & -(\gamma+\mu_1) & 0 & 0 \\ 0 & 0 & -\mu_2 & \\ 0 & \varphi_2 & -\mu_2 & \end{pmatrix}$$

$$V^{-1} = \begin{bmatrix} \frac{1}{N_1} & 0 & 0 & 0 \\ \frac{-N_2}{N_1 N_3} & \frac{1}{N_3} & 0 & 0 \\ 0 & 0 & \frac{1}{N_4} & 0 \\ 0 & 0 & \frac{1}{N_4 N_6} & \frac{1}{N_6} \end{bmatrix}$$

Where constants $N_1 = -(\delta_1 + \mu_1)$, $N_2 = \sigma_1$, $N_3 = -(\gamma + \mu_{1t_\delta})$, $N_4 = -\mu_2$, $N_6 = -\mu_2$, $N_5 = \varphi_2$

$$FV^{-1} = \begin{bmatrix} 0 & 0 & \frac{\propto_1 \frac{S_H}{N_H}}{N_4 N_6} & \frac{\propto_1 \frac{S_H}{N_H}}{N_6} \\ 0 & 0 & 0 & 0 \\ \frac{-\frac{\alpha_2 s_m}{N_H} N_2}{N_1 N_3} & \frac{\frac{\alpha_2 s_m}{N_H}}{N_3} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

$$\text{Then, } |FV^{-1} - \lambda I| = \begin{vmatrix} -\lambda & 0 & \frac{\propto_1 \frac{S_H}{N_H}}{N_4 N_6} & \frac{\propto_1 \frac{S_H}{N_H}}{N_6} \\ 0 & -\lambda & 0 & 0 \\ \frac{-\frac{\alpha_2 s_m}{N_H} N_2}{N_1 N_3} & \frac{\frac{\alpha_2 s_m}{N_H}}{N_3} & -\lambda & 0 \\ 0 & 0 & 0 & -\lambda \end{vmatrix} = 0$$

$\lambda_1 = 0$

$\lambda_2 = 0$

$$\lambda_{3,4} = \sqrt{\frac{\frac{\alpha_2 s_m}{N_H} N_2}{N_1 N_3} + \frac{\propto_1 \frac{S_H}{N_H}}{N_4 N_6}}$$

The reproductive number $R_C = \rho\left(FV^{-1}\right) = \sqrt{\frac{\frac{\alpha_2 s_m}{N_H} N_2}{N_1 N_3} + \frac{\propto_1 \frac{S_H}{N_H}}{N_4 N_6}}$

Here, the effective reproductive number R_c is the spectral radius (dominant eigenvalue) of the product matrix FV^{-1}

4.4 Stability of the disease free equilibrium

Theorem 1. The model (1) to (7) is local asymptotically if the effective reproductive number $R_c < 1$.

Proof

Theorem 1 will be proved the Eigen-values of the Jacobian matrix evaluated at DFE.

$$J_0 = \begin{bmatrix} R_1 & 0 & R_5 & R_9 & 0 & 0 & R_{15} \\ R_2 & R_3 & 0 & 0 & 0 & 0 & R_{16} \\ 0 & R_4 & R_6 & R_{10} & 0 & 0 & 0 \\ 0 & 0 & R_7 & R_{11} & 0 & 0 & 0 \\ 0 & 0 & R_8 & 0 & R_{12} & 0 & 0 \\ 0 & 0 & 0 & 0 & R_{13} & R_{14} & R_{17} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$|J_0 - \boldsymbol{\lambda I}| = \begin{vmatrix} R_1 - \boldsymbol{\lambda} & 0 & R_5 & R_9 & 0 & 0 & R_{15} \\ R_2 & R_3 - \boldsymbol{\lambda} & 0 & 0 & 0 & 0 & R_{16} \\ 0 & R_4 & R_6 - \boldsymbol{\lambda} & R_{10} & 0 & 0 & 0 \\ 0 & 0 & R_7 & R_{11} - \boldsymbol{\lambda} & 0 & 0 & 0 \\ 0 & 0 & R_8 & 0 & R_{12} - \boldsymbol{\lambda} & 0 & 0 \\ 0 & 0 & 0 & 0 & R_{13} & R_{14} - \boldsymbol{\lambda} & R_{17} \\ 0 & 0 & 0 & 0 & 0 & 0 & -\boldsymbol{\lambda} \end{vmatrix} = 0$$

$(R_1 - \boldsymbol{\lambda})(R_3 - \boldsymbol{\lambda})(R_6 - \boldsymbol{\lambda})(R_{11} - \boldsymbol{\lambda})(R_{12} - \boldsymbol{\lambda})(R_{14} - \boldsymbol{\lambda})(-\boldsymbol{\lambda}) = 0$

$\boldsymbol{\lambda = 0}$

$\boldsymbol{\lambda} = R_1 = -\alpha_1 I_m - \mu_1$

$\boldsymbol{\lambda} = R_3 = -(\sigma_1 + \mu_1)$

$\boldsymbol{\lambda} = R_6 = -(\gamma + \mu_1 \gamma)$

$\boldsymbol{\lambda} = R_{11} = -(\gamma + \rho)$

$\boldsymbol{\lambda} = R_{12} = -\dfrac{\alpha_2 I_H}{N_H} - \mu_2$

$\boldsymbol{\lambda} = R_{14} = -\mu_2$

Since ALL of the Eigen-values of the Jacobin are all negative, we conclude that the DFE of the model is locally asymptotically stable whenever $R_c < 1$.

CHAPTER FIVE

DISCUSSIONS, SUMMARY AND RECOMMENDATIONS

5.0 Introduction

This chapter includes discussion of the study, summary of the study and recommendations for further studies.

5.1 Discussion of the study

The main participants of this study were employees, and management of Jinja referral hospital in Jinja district and the hospital data base and patient records were referred to in this study.

When research was conducted in general case diseases department, it was found out that malaria was the common disease in this hospital in fact results found out that there is common disease of malaria in Jinja district and the results are remorse to the community.

Malaria is an important public health in our country. It is global threat to health and socioeconomic development. It affects about 300 million people and cause a million deaths per year worldwide (Muhammad Idris et al, 2007). Earlier diagnosis and prompt treatment is crucial for prevention its complications. It affects all the age groups and both male and female gender. In this study plasmodium vivax and falciferum were the commonest type of parasites detected. Malaria was more frequent in pediatric age group constituting about half of the cases and more in age group 45 to 80 years.

In 2016, an estimated 263 cases of malaria occurred in district (95% confidence interval [CI]: 196–263 cases), compared with 237 cases in 2010 (95% CI: 218–278 cases) and 211 cases in 2015 (95% CI: 192–257).Most malaria cases in 2016 were in the eastern Region of Uganda (90%), followed by the South-East Region (7%) and the middle Region of Jinja (2%). Of the medicinal report reporting indigenous malaria cases in 2016, except Jinja – carried 80% of the malaria burden.

The incidence rate of malaria is estimated to have decreased by 18% globally, from 76 to 63 cases per 1000 population at risk, between 2010 and 2016. The Jinja Region recorded the largest

increase (48%) followed by the other areas. Despite these reductions, between 2014 and 2016, substantial increases in case incidence occurred in the district, and marginally in the regions.Plasmodium falciparum is the most prevalent malaria parasite in Uganda, accounting for 99% of estimated malaria cases in 2016. Outside of Jinja district, P. vivax is the predominant parasite in the Jinja districts, representing 64% of malaria cases.

Malaria deaths. In 2016, there were an estimated 300 deaths from malaria in Jinja district, compared to 446 estimated deaths in 2015. The Jinja district accounted for 91% of all malaria deaths in 2016, followed by the national medical report (6%) increase.All regions recorded reductions in mortality in 2016 when compared with 2010, with the exception of the district as Region, where mortality rates remained virtually unchanged in the period. The largest decline occurred in the national report (44%), Jinja district (37%). However, between 2015 and 2016, mortality rates stalled in the regions.

5.2 Summary of the Study

In this report we have developed mathematical model for the transmission of malaria by considering recurrent infection. The disease free and endemic equilibrium, basic reproductive number and stability is presented.