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Modelling Transmission of Buruli Ulcer in the Central Region of Ghana

Nyarko Christiana Cynthia, Nyarko Peter Kwesi, Ampofi Isaac, Asante Emmanuel

Mathematical Sciences Department, University of Mine and Technology, Tarkwa, Ghana

Email address:
ccnyarko@umat.edu.gh (N. C. Cynthia)

Abstract: The pathogen of Buruli Ulcer (BU) is known to be Mycobacterium Ulcerans whose mode of transmission is entirely not known, although the disease is recognised to be associated with contaminated water. The hypothesised transmission involves humans being bitten by the water bugs (vector) that prey on mollusks, snails and young fishes. The hypothesised transmission also involves humans feeding on an infected fish or frog. This study seeks to contribute to the dynamics and analyses of the transmission mechanism of Buruli Ulcer in communities along Offin River in the Central Region of Ghana. The model equilibria were determined and conditions for the equilibria were also established. The basic reproduction number, R_0 was derived using the Next Generation approach and its estimated value was 1.20771. The result reveals that, R_0 is greater than 1, indicating a horizontal spread of the infection across the population. The transmission dynamics of Buruli Ulcer model of the Susceptible, Infected and Recovered (SIR) type also show that the disease will continue to spread at the study areas as long as the reservoir for Mycobacterium Ulcerans continue to sustain enough infected water bugs and infected fish or infected frog to contain the disease. The study further concludes that, the rate of spread of Buruli Ulcer in the affected communities continue to be high due to its mode of transmission. This study suggest that adequate control measures including mass education and prompt treatment to curb the spread should be emphasized.

Keywords: Pathogen, Buruli, Ulcer, Ulcerans, Spread, Infected, Stagnant, Humans, Vector

1. Introduction

Modelling of infectious disease is a tool which has been used to study the means by which diseases spread, forecast the future course of an outbreak and to evaluate strategies to control an epidemic [1]. Mathematical models may not offer comprehensive descriptions of how to control diseases. They are elegant methods for evaluating the possible influence of different strategies offered in public health intervention programs [2].

Buruli Ulcer (BU) is a disease of the skin caused by Mycobacterium Ulcerans, a slow growing mycobacterium that classically infect the skin and subcutaneous tissue, giving rise to indolent no ulcerated (nodules, plaques) and ulcerated lesions. After tuberculosis and leprosy, Buruli Ulcer is the third most common mycobacteriosis of human. The mode of Mycobacterium Ulcerans transmission is not fully understood in the study area, although the disease is recognized to be associated to contaminated water. Areas affected by Buruli Ulcer disease are located near stagnant or slow-moving water, and outbreaks appear to be related to environmental changes (deforestation, agriculture, hydraulic installations) involving surface water [3].

The occurrence of Buruli Ulcer upstream of the Offin River is greater and steeply dwindles as you go beyond Dunkwa. So, the communities on the upstream of river Offin from Agroyesum (e.g. Subin, Ameyaw, Betenase, Ampabena, Nkotumso, Dominase, Ayanfuri, Powerline, Obiarabiaradanedanmu, Pokukrom and Dunkwa) are very endemic [3]. Therefore, to provide awareness of this endemic, this paper seeks to develop a transmission model (deterministic model) of Buruli Ulcer and help to identify control measures that will minimize the disease in the study area.

2. Literature Review

In Africa, the history of Buruli Ulcer can be divided into two main periods: before 1980 and after 1980. There were many important literatures before 1980 on the disease in

several African countries: Cameroon, the Democratic Republic of the Congo, Gabon, Ghana, Nigeria and Uganda. In the Central African Republic, Kenya, Sudan, and the United Republic of Tanzania, cases were suspected but never confirmed. The most significant contributions came from the Democratic Republic of the Congo and Uganda. The Uganda Buruli Group studied the clinic pathological and epidemiological aspects of the disease extensively, and opted for the term "Buruli Ulcer" because large numbers of cases were first detected in the district of Buruli near Lake Kyoga [4].

After 1980, new foci of Buruli Ulcer emerged in West Africa. A dramatic increase in the incidence of the disease is now reported in several West Africa countries, especially in Benin, Cote d'Ivoire and Ghana [5].
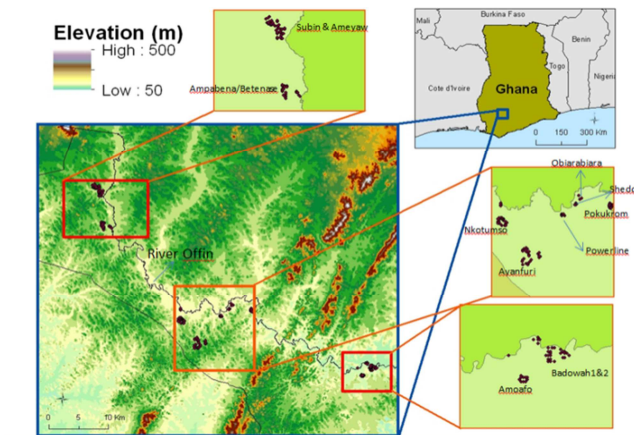

Figure 1. Study Communities (Source [3]).

The communities along Offin River in the Central Region of Ghana are endemic to Buruli Ulcer disease. Figure 1 present the communities along Offin River. These areas of study are located near stagnant or slow-moving water, and experience similar environmental changes (deforestation, agriculture, and mining) involving surface water. The primary means of securing the necessities of life in these communities are farming and mining [3]. It can be seen from the Powerline community (Figure 2), most of the cases are in Zones 3 and 4 and also at the fringes of the community. Communities such as Betenase, Ampabena (Figure 1) have Buruli Ulcer cases all over the community which seems to portray that the whole community is endemic.

Figure 3 portrays that Zone 1 of Ayamfuri has about 70% of Buruli Ulcer cases and even in that zone, 90% were clustered together in a small sector within the centre of the town.
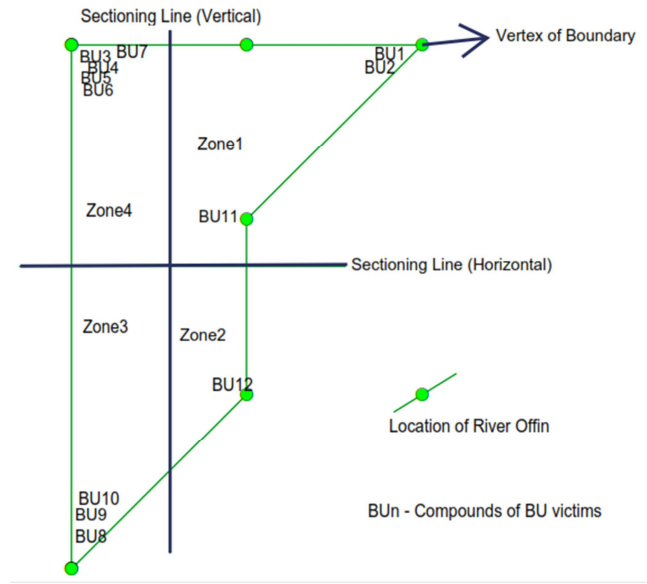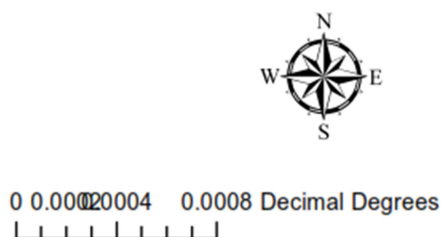

Figure 2. Map of Powerline (Source [3]).

Scot proposed a mathematical model of the SIR-type in an endeavour to explain the role of aquatic insects and arsenic in the spread of Buruli ulcer disease [6]. The paper considered arsenic environment as a reservoir for Mycobacterium ulcerans and water bug (vector) for Buruli Ulcer disease. In their model, they proposed that Buruli Ulcer is a micro parasitic disease in which host parasite interaction basically occurs within isolated communities. Again, it was assumed that the host population is of fixed size containing susceptible individuals who are not yet infected with Mycobacterium Ulcerans. It also assumed humans who develop Buruli Ulcer become immune to any further attack and this assumption led them to the SIR model. The model equations describing the proportion of humans infected by Mycobacterium Ulcerans and the corresponding proportion of water-bugs according to them are given by:

$$\left.\begin{aligned} \frac{dx}{dt} &= maby(1-x) - rx \\ \frac{dy}{dt} &= a_1 x(1-y) - (\mu - \alpha)y \end{aligned}\right\} \quad (1)$$

Table 1. Description of Parameters used in the Equation (1).

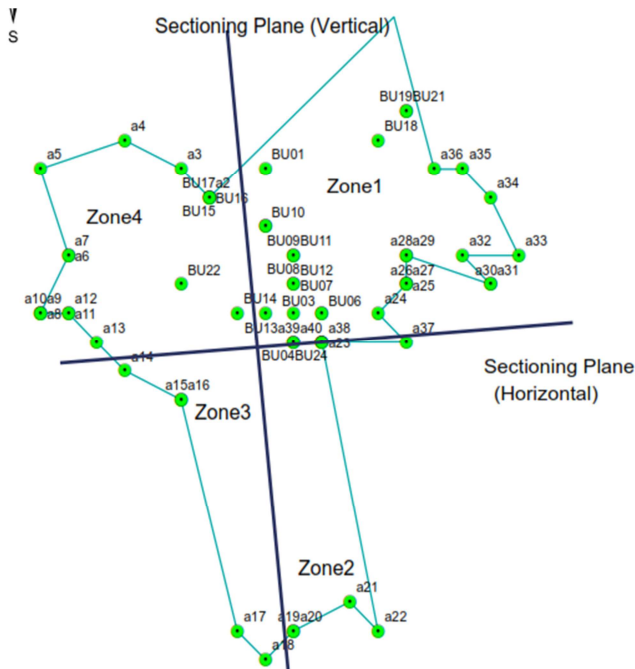| Symbol	Description
m	Density of water bugs (Number of water bugs per human host)
a	Bite frequency (biting rate of human by single water-bug)
a_1	Rate of ingestion of MU by water bugs
b	Proportion of infected bites on humans that produce infection
α	Relative concentration as in water
μ	Mortality rate of water-bugs
x	Proportion of humans infected by MU
y	Proportion of water-bugs infected by MU
r	Death rate of humans

Figure 3. Map of Ayanfuri (Source [3]).

The study displayed a nonlinear relationship between the basic reproductive number (R_0) and the widespread of infection of both infected water bugs and infected humans at a particular time. However, a small increase in the reproductive number lead to a large change in both the prevalence levels of humans and water bugs. It was deduce from their graph that, higher levels of (R_0) will lead to increases in cases of Buruli Ulcer for $R_0 > 1$. Thus, if Buruli

Ulcer is not controlled it will continue to spread in regions with unconducive conditions. Nyabadza and Bonyah develop the transmission dynamics of Buruli Ulcer in Ghana: Insights through a mathematical model [7]. In their paper, a model for the transmission of Mycobacterium Ulcerans to human in the presence of a preventive strategy was proposed and analysed. The model equilibria were determined and conditions for the existence of the equilibria established. The model analysis was carried out in terms of the reproduction number R_0. The disease-free equilibrium was found to be locally asymptotically stable for $R_0 < 1$. The model was then fitted to data from Ghana. The dynamics of the disease was described by the following set of nonlinear set differential equations;

$$
\begin{aligned}
\frac{dS_H}{dt} &= \mu_H N_H + \theta R_H - \frac{\beta_H S_H I_V}{N_H} - \mu_H S_H \\
\frac{dI_H}{dt} &= \frac{\beta_H S_H I_V}{N_H} - (\gamma + \mu_H) I_H \\
\frac{dR_H}{dt} &= \gamma I_H - (\theta + \mu_H) R_H \\
\frac{dS_V}{dt} &= \mu_V N_V - \frac{\beta_V S_V I_F}{N_V} - \frac{\eta_V \beta_V S_V U}{K} - \mu_V S_V \\
\frac{dI_V}{dt} &= \frac{\beta_V S_V I_F}{N_V} + \frac{\eta_V \beta_V S_V U}{K} - \mu_V I_V \\
\frac{dS_F}{dt} &= \mu_F N_F - \frac{\beta_F I_F U}{K} - \frac{\eta_F \beta_F I_F U}{K} - \mu_F S_F \\
\frac{dI_F}{dt} &= \frac{\beta_F I_F U}{K} + \frac{\eta_F \beta_F I_F U}{K} - \mu_F I_F \\
\frac{dU_M}{dt} &= \sigma_F I_F + \sigma_V I_V - \mu_E U
\end{aligned}
\qquad (2)
$$

Table 2. Description of parameters used in Equation (2).

Symbol	Description
β_H	The effective contact rate between the vector and susceptible human
β_V	The effective contact rate between fish and susceptible vector
β_F	The effective contact rate between the susceptible fish and Mycobacterium Ulcerans
γ	The recovery rate of infected humans
θ	The rate of loss of immunity of recovered humans
μ_H	Birth rate of the human population
μ_V	Birth rate of the vector population
μ_F	Birth rate of the fish population
rV	The growth rate of the vector population
rF	The growth rate of the fish population
K	The environmental carrying capacity of the bacteria population
σ_F	Rate of shedding of Mycobacterium Ulcerans into the environment by fish-frog
σ_V	Rate of shedding of Mycobacterium Ulcerans into the environment by the vector
μ_E	Rate at which Mycobacterium Ulcerans are cleared from the environment.

The model exhibits a backward bifurcation and the endemic equilibrium point is globally stable when $R_0 < 1$. Sensitivity analysis also showed that the Buruli Ulcer epidemic is highly influenced by the shedding and clearance rates of Mycobacterium Ulcerans in the environment. The model was found to fit reasonably well to data from Ghana and projections on the future of the Buruli Ulcer epidemic were also made.

3. Methodology

A constant human population $P_H(t)$, the vector population of insect (e.g. water bugs, mosquitoes etc.) $P_V(t)$, the fish-frog population, $P_{FF}(t)$ at any time (t) was considered. The

total human population is divided into three epidemiological subclasses of those that are susceptible $S_H(t)$, the infected $I_H(t)$ and the recovered who is able to resist the infection owning to the presence of a particular treatment $R_H(t)$. Total vector population at any time t is divided into two subclasses of those that are susceptible vector $S_V(t)$ and those that are infectious and can transmit the Buruli ulcer to humans $I_V(t)$. The total population reservoir of fish-frog is also divided into two compartments of susceptible fish $S_{FF}(t)$ and infected fish $I_{FF}(t)$. Consideration of the role of the environment was made by introducing a compartment U_M, representing the density of Mycobacterium Ulcerans in the environment. Assumptions of the model is;

Mycobacterium Ulcerans are transferred from vector (water bug), fish and frog to the humans.

There is homogeneity of human, vector and fish-frog population's interactions.

Infected humans recover and are temporarily immune, but eventually lose immunity.

Fish and amphibian (frog) are preyed on by the vector and the human.

The acquiring of Mycobacterium Ulcerans through environmental contact and direct person-to-person transmission is rare [8].

Susceptible host are more likely to be infected by the disease through biting by an infectious vector (water bug). β_H Being the effective biting rate that an infectious vector has to susceptible host and $(\beta_H S_H I_V)/P_H$ being the incidence of new infections transmitted by a vector. $(\beta_H S_H I_{FF})/P_H$ Being the incidence of new infections transmitted to a human when the human prayed on an infected fish or frog.

Susceptible insect is infected at a rate $(\beta_V S_V I_{FF})/P_V$ through the predation of infected fish or frog and $(\eta \beta_V S_V U_M)/K$ representing other sources in the environment. Where η differentiates the infectivity potential of the fish-frog from that of the environment.

The vector population and the fish-frog population are assumed to be constant. Their growth functions are given by $g(P_V)$ and $g(P_{FF})$ respectively. Generally, we can assume that $g(P_V) = \mu_V P_V$ and $g(P_{FF}) = \mu_F P_{FF}$.

There is a proposed hypothesis that environmental mycobacteria in the bottoms of swamps may mechanically concentrated by small water-filtering organisms such as microphagous fish, snails, mosquito larvae, small crustaceans and protozoa [9]. It can therefore be assumed that fish-frog increase the environmental concentrations of mycobacterium Ulcerans at a rate σ_{FF}. Humans are assumed not to shed any bacteria into the environment.

Vector release bacteria into the environment at a rate σ_V.

The model does not include a potential route of direct contact with the bacterium in water.

The birth rate of the human population is directly proportional to the size of the human population.
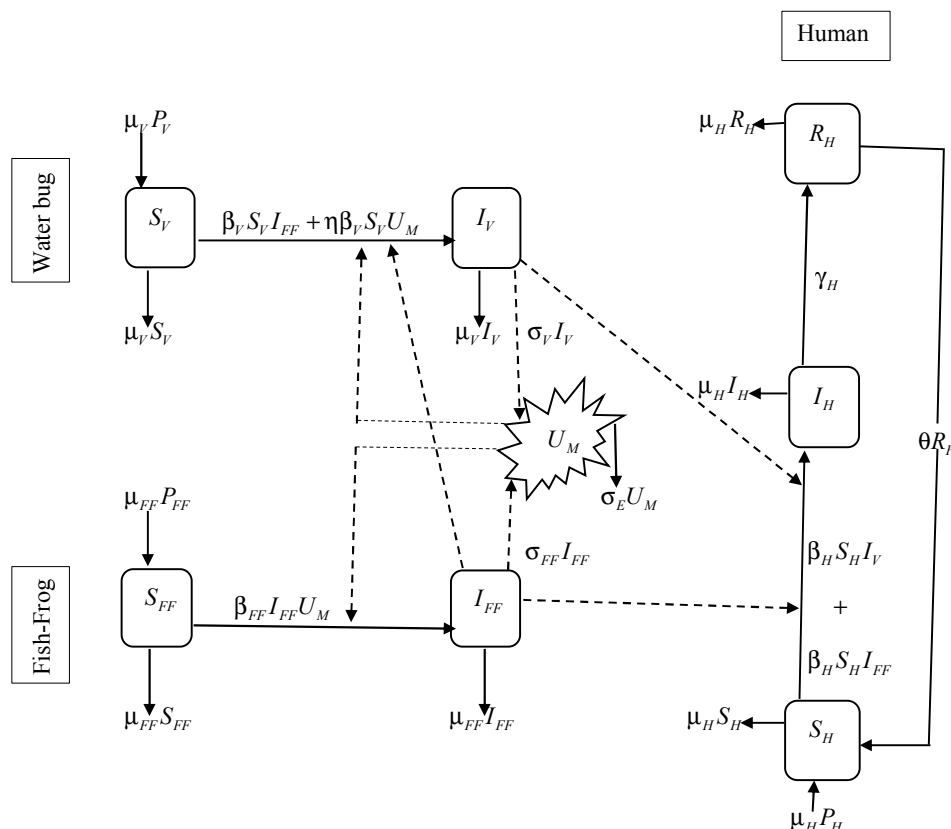

Figure 4. Transmission Dynamics of Buruli Ulcer among Fish-Frog, Water bug and Human.

Hence the dynamics of Buruli ulcer can be described by the following set of nonlinear differential equations;

$$
\left.\begin{array}{l}
\dfrac{dS_H}{dt} = \mu_H P_H + \theta R_H - \dfrac{\beta_H S_H I_V}{P_H} - \dfrac{\beta_H S_H I_{FF}}{P_H} - \mu_H S_H \\[2mm]
\dfrac{dI_H}{dt} = \dfrac{\beta_H S_H I_V}{P_H} + \dfrac{\beta_H S_H I_{FF}}{P_H} - (\gamma + \mu_H) I_H \\[2mm]
\dfrac{dR_H}{dt} = \gamma I_H - (\theta + \mu_H) R_H \\[2mm]
\dfrac{dS_V}{dt} = \mu_V P_V - \dfrac{\beta_V S_V I_{FF}}{P_V} - \dfrac{\eta \beta_V S_V U_M}{K} - \mu_V S_V \\[2mm]
\dfrac{dI_V}{dt} = \dfrac{\beta_V S_V I_{FF}}{P_V} + \dfrac{\eta \beta_V S_V U_M}{K} - \mu_V I_V \\[2mm]
\dfrac{dS_{FF}}{dt} = \mu_{FF} P_{FF} - \dfrac{\beta_{FF} I_{FF} U_M}{K} - \mu_{FF} S_{FF} \\[2mm]
\dfrac{dI_{FF}}{dt} = \dfrac{\beta_{FF} I_{FF} U_M}{K} - \mu_{FF} I_{FF} \\[2mm]
\dfrac{dU_M}{dt} = \sigma_{FF} I_{FF} + \sigma_V I_V - \mu_E U_M
\end{array}\right\} \quad (3)
$$

3.1. Positivity of Solution in Equation (3)

Let $t_1 = \sup(t > 0 \mid S_H > 0$, $I_H > 0$, $R_H > 0$, $S_V > 0$, $I_V > 0$, $S_{FF} > 0$, $I_{FF} > 0$ and $U_M > 0) \in [0, t]$

Considering the susceptible human compartment of Equation (3.6) of the model,

$$\frac{dS_H}{dt} \geq \mu_H P_H + \theta R_H - \frac{\beta_H S_H I_V}{P_H} - \frac{\beta_H S_H I_{FF}}{P_H} - \mu_H S_H \quad (3)$$

Factorising S_H out of Equation (3) gives Equation (4)

$$\frac{dS_H}{dt} \geq \mu_H P_H + \theta R_H - \left(\frac{\beta_H I_V}{P_H} + \frac{\beta_H I_{FF}}{P_H} + \mu_H\right) S_H \quad (4)$$

Let

$$\lambda_1 = \frac{\beta_H I_V}{P_H} > 0 \quad (5)$$

and

$$\lambda_2 = \frac{\beta_H I_{FF}}{P_H} > 0 \quad (6)$$

Substituting Equation (5) and Equation (6) into Equation (4), one can obtain Equation (7)

$$\frac{dS_H}{dt} \geq \mu_H P_H + \theta R_H - (\lambda_1 + \lambda_2 + \mu_H) S_H \quad (7)$$

Equation (7) can further be expressed as Equation (8)

$$\frac{dS_H}{dt} + (\lambda_1 + \lambda_2 + \mu_H) S_H \geq \mu_H P_H + \theta R_H \quad (8)$$

Seeking for an integrating factor (IF)

$$IF = \exp\left[\int_0^t (\lambda_1 + \lambda_2 + \mu_H) dt\right] \quad (9)$$

Hence Equation (9) can therefore be simplified as Equation (10)

$$IF = \exp\left\{\int_0^t [\lambda_1(s) + \lambda_2(s)] ds + (\mu_H) t\right\} \quad (10)$$

Multiplying through Equation (10) by Equation (8) gives Equation (11)

$$
\left.\begin{array}{l}
\exp\left\{\int_0^t [\lambda_1(s) + \lambda_2(s)] ds + (\mu_H) t\right\} \dfrac{dS_H}{dt} + \\[3mm]
\exp\left\{\int_0^t [\lambda_1(s) + \lambda_2(s)] ds + (\mu_H) t\right\} (\lambda_1 + \lambda_2 + \mu_H) S_H \\[3mm]
\geq \exp\left\{\int_0^t [\lambda_1(s) + \lambda_2(s)] ds + (\mu_H) t\right\} (\mu_H P_H + \theta R_H)
\end{array}\right\} \quad (11)
$$

Equation (12) is obtained by simplifying Equation (11)

$$
\left.\begin{array}{l}
\dfrac{d}{dt}\left[S_H(t) \exp\left\{\int_0^t [\lambda_1(s) + \lambda_2(s)] ds + (\mu_H) t\right\} \right] \\[3mm]
\geq (\mu_H P_H + \theta R_H) \exp\left\{\int_0^t [\lambda_1(s) + \lambda_2(s)] ds + (\mu_H) t\right\}
\end{array}\right\} \quad (12)
$$

Equation (13) is also obtained by Multiplying Equation (12) by dt

$$
\left.\begin{array}{l}
d\left[S_H(t) \exp\left\{\int_0^t [\lambda_1(s) + \lambda_2(s)] ds + (\mu_H) t\right\} \right] \\[3mm]
\geq \left[(\mu_H P_H + \theta R_H) \exp\left\{\int_0^t [\lambda_1(s) + \lambda_2(s)] ds + (\mu_H) t\right\} \right] dt
\end{array}\right\} \quad (13)
$$

Integrating both sides of Equation (13), one obtains equation (14)

$$
\left.\begin{array}{l}
S_H(\hat{t}) \exp\left\{\int_0^{\hat{t}} [\lambda_1(s) + \lambda_2(s)] ds + (\mu_H) \hat{t}\right\} \\[3mm]
\geq \int_0^{\hat{t}} \left[(\mu_H P_H + \theta R_H) \exp\left\{\int_0^{\hat{t}} [\lambda_1(z) + \lambda_2(z)] dz + (\mu_H) \hat{t}\right\} \right] d\hat{t} + S(0)
\end{array}\right\} \quad (14)
$$

Dividing Equation (3.18) by $\exp\left\{\int_0^{\hat{t}}[\lambda_1(s)+\lambda_2(s)]ds+(\mu_H)\hat{t}\right\}$ and simplifying further, Equation (14) then becomes Equation (15)

$$
S_H(\hat{t}) \geq S(0)\exp\left[-\left\{\int_0^{\hat{t}}[\lambda_1(s)+\lambda_2(s)]ds+(\mu_H)\hat{t}\right\}\right]+
$$
$$
\exp\left[-\left\{\int_0^{\hat{t}}[\lambda_1(s)+\lambda_2(s)]ds+(\mu_H)\hat{t}\right\}\right]\times
$$
$$
\int_0^{\hat{t}}\left[(\mu_H P_H+\theta R_H)\exp\left\{\int_0^{\hat{t}}[\lambda_1(z)+\lambda_2(z)]dz+(\mu_H)\hat{t}\right\}\right]d\hat{t}
\tag{15}
$$

The right-hand side of Equation (15) is positive, which can be expressed as Equation (16)

$$
\left.\begin{aligned}
& S(0)\exp\left[-\left\{\int_0^{\hat{t}}[\lambda_1(s)+\lambda_2(s)]ds+(\mu_H)\hat{t}\right\}\right]+ \\
& \exp\left[-\left\{\int_0^{\hat{t}}[\lambda_1(s)+\lambda_2(s)]ds+(\mu_H)\hat{t}\right\}\right]\times \\
& \int_0^{\hat{t}}\left[(\mu_H P_H+\theta R_H)\exp\left\{\int_0^{\hat{t}}[\lambda_1(z)+\lambda_2(z)]dz+(\mu_H)\hat{t}\right\}\right]d\hat{t}
\end{aligned}\right\} > 0
\tag{16}
$$

From Equation (16), it can be concluded that $S_H(\hat{t})$ is positive and it is given by Equation (17) below

$$
S_H(\hat{t}) > 0 \tag{17}
$$

Similarly, it can be shown that $I_H(0) > 0$, $R_H(0) > 0$, $S_V(0) > 0$, $I_V(0) > 0$, $S_{FF}(0) > 0$, $I_{FF}(0) > 0$ and

$U_M(0) > 0$ for all $t > 0$.

3.2. Identification of the Biological Interest of the Model

The biological region of interest of Equation (3) is given as Equation (18)

$$
\left.\begin{aligned}
& D_H = \left\{(S_H, I_H, R_H)\in\mathbb{R}_+^3 : S_H+I_H+R_H \leq \frac{P_H}{\mu_H}\right\} \\
& D_V = \left\{(S_V, I_V)\in\mathbb{R}_+^2 : S_V+I_V \leq \frac{P_V}{\mu_V}\right\} \\
& D_{FF} = \left\{(S_{FF}, I_{FF})\in\mathbb{R}_+^2 : S_{FF}+I_{FF} \leq \frac{P_{FF}}{\mu_{FF}}\right\} \\
& D_{U_M} = 0 < U_M < \frac{P_{FF}}{\mu_{FF}} \\
& \Omega = \left\{(S_H, I_H, R_H, S_V, I_V, S_{FF}, I_{FF}, U_M)\in\mathbb{R}_+^8 \mid S_H+I_H+R_H = P_H\right\}
\end{aligned}\right\}
\tag{18}
$$

where P_H is constant.

The above model (3.6) can be solved by equating the right-hand side of the model to zero. This computation shows that the model always has a disease free equilibrium (DFE) at $E_0 = (S_H^0, 0, 0, S_V^0, 0, S_{FF}^0, 0, 0)$ where, $S_H = P_H$, $I_H = 0$, $R_H = 0$, $S_V = P_V$, $I_V = 0$, $S_{FF} = P_{FF}$, $I_{FF} = 0$ and $U_M = 0$ and a unique endemic equilibrium $E_{ee} = (S_H^1, I_H^1, R_H^1, S_V^1, I_V^1, S_{FF}^1, I_{FF}^1, U_M^1)$ in Ω.

The basic reproduction number (R_0) is defined as the average number of new cases of an infection caused by one typical infected individual in a population consisting of susceptible only [10].

To calculate R_0 for the above model using the Next Generation Operator approach we let T be the state of the disease or the transmission state of the disease of Equation (3).

The transmission state of Equation (3) is given by Equation (19)

$$T_1 = \frac{\beta_H S_H I_V}{P_V} + \frac{\beta_H S_H I_{FF}}{P_H}$$
$$T_2 = \frac{\beta_V S_V I_{FF}}{P_V} + \frac{\eta \beta_V S_V U_M}{K}$$
$$T_3 = \frac{\beta_{FF} I_{FF} U_M}{K}$$

$$(19)$$

Taking the Jacobian matrix of T_1, T_2 and T_3 with respect to I_H, I_V, I_{FF} and U_M gives, one can obtain Equation (20) below

$$T = \begin{pmatrix} 0 & \dfrac{\beta_H S_H}{P_H} & \dfrac{\beta_H S_H}{P_H} & 0 \\ 0 & 0 & \dfrac{\beta_V S_V}{P_V} & \dfrac{\eta \beta_V S_V}{K} \\ 0 & 0 & \dfrac{\beta_{FF} U_M}{K} & \dfrac{\beta_{FF} I_{FF}}{K} \\ 0 & 0 & 0 & 0 \end{pmatrix} \quad (20)$$

Evaluating T at the disease-free equilibrium also gives Equation (21)

$$T = \begin{pmatrix} 0 & \beta_H & \beta_H & 0 \\ 0 & 0 & \beta_V & \dfrac{\eta \beta_V P_V}{K} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \quad (21)$$

Let $\sum$ be the transition state of Equation (3).

Hence the transition state of the disease can be expressed as Equation (22)

$$V_1 = -(\gamma + \mu_H)$$
$$V_2 = -\mu_V I_V$$
$$V_3 = -\mu_{FF} I_{FF}$$
$$V_4 = \sigma_V I_V + \sigma_{FF} I_{FF} - \mu_E U_M$$

$$(22)$$

Taking the Jacobian matrix of V_1, V_2, V_3, and V_4 with respect to I_H, I_V, I_{FF} and U_M gives

$$\sum = \begin{pmatrix} -(\gamma + \mu_H) & 0 & 0 & 0 \\ 0 & -\mu_V & 0 & 0 \\ 0 & 0 & -\mu_{FF} & 0 \\ 0 & \sigma_V & \sigma_{FF} & -\mu_E \end{pmatrix} \quad (23)$$

From Equation (23), we have Equation (24)

$$-\sum = \begin{pmatrix} (\gamma + \mu_H) & 0 & 0 & 0 \\ 0 & \mu_V & 0 & 0 \\ 0 & 0 & \mu_{FF} & 0 \\ 0 & -\sigma_V & -\sigma_{FF} & \mu_E \end{pmatrix} \quad (24)$$

Hence the inverse of Equation (24) is computed as Equation (25)

$$-\sum{}^{-1} = \begin{pmatrix} \dfrac{1}{(\gamma + \mu_H)} & 0 & 0 & 0 \\ 0 & \dfrac{1}{\mu_V} & 0 & 0 \\ 0 & 0 & \dfrac{1}{\mu_{FF}} & 0 \\ 0 & \dfrac{\sigma_V}{\mu_V \mu_E} & \dfrac{\sigma_{FF}}{\mu_{FF} \mu_E} & \dfrac{1}{\mu_E} \end{pmatrix} \quad (25)$$

Let K_L = Next Generation Matrix (NGM) with large domain. Therefore, the NGM is computed as Equation (26)

$$K_L = -T \sum{}^{-1} \quad (26)$$

hence

$$K_L = \begin{pmatrix} 0 & \beta_H & \beta_H & 0 \\ 0 & 0 & \beta_V & \dfrac{\eta \beta_V P_V}{K} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} \dfrac{1}{(\gamma + \mu_H)} & 0 & 0 & 0 \\ 0 & \dfrac{1}{\mu_V} & 0 & 0 \\ 0 & 0 & \dfrac{1}{\mu_{FF}} & 0 \\ 0 & \dfrac{\sigma_V}{\mu_V \mu_E} & \dfrac{\sigma_{FF}}{\mu_{FF} \mu_E} & \dfrac{1}{\mu_E} \end{pmatrix} \quad (27)$$

Simplifying Equation (27) above gives Equation (28) below

$$K_L = \begin{pmatrix} 0 & \dfrac{\beta_H}{\mu_H} & \dfrac{\beta_H}{\mu_{FF}} & 0 \\ 0 & \dfrac{\eta \beta_V P_V \sigma_V}{K \mu_V \mu_E} & \dfrac{\beta_V}{\mu_{VV}} + \dfrac{\eta \beta_V P_V \sigma_{FF}}{K \mu_{FF} \mu_E} & \dfrac{\eta \beta_V P_V}{K \mu_E} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \quad (28)$$

Let λ_n be the eigenvalues of K_L. Then the eigenvalues of Equation (28) is computed as Equation (29)

$$\det(K_L - \lambda I) = 0 \quad (29)$$

Where I is a 4×4 identity matrix and $n = 1, 2, 3, 4$.

Hence the eigenvalues of Equation (28) are obtained as Equation (30)

$$\lambda_1 = 0$$
$$\lambda_2 = 0$$
$$\lambda_3 = 0 \tag{30}$$
$$\lambda_4 = \frac{\eta \beta_V P_V \sigma_V}{K \mu_V \mu_E}$$

The basic reproductive number (R_0) is the spectral radius of K_L which is written as Equation (31)

$$R_0 = \rho(K_L) \tag{31}$$

Hence the basic reproduction number is largest eigenvalue of Equation (30).

Therefore

$$R_0 = \lambda_4 \tag{32}$$

Hence the basic reproduction number is given by Equation (33)

$$R_0 = \frac{\eta \beta_V P_V \sigma_V}{K \mu_V \mu_E} \tag{33}$$

The basic reproduction number of the model is determined by the vector population, the density of Mycobacterium Ulcerans in the environment and the infected Fish-Frog population from that environment. The R_0 actually appears to be influenced by the rate at which Mycobacterium Ulcerans is introduced into the environment and the infectivity potential of the Fish-Frog from that of the environment.

3.3. The Stability of the Disease-Free Equilibrium (DFE)

Let J_{E_0} be the Jacobian evaluated at DFE of the model, therefore

$$J_{E_0} = \begin{pmatrix} -\mu_H & 0 & \theta & 0 & -\beta_H & 0 & -\beta_H & 0 \\ 0 & -(\gamma + \mu_H) & 0 & 0 & \beta_H & 0 & \beta_H & 0 \\ 0 & \gamma & -(\theta + \mu_H) & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\mu_V & 0 & 0 & -\beta_V & -\frac{\eta \beta_V P_V}{K} \\ 0 & 0 & 0 & 0 & -\mu_V & 0 & \beta_V & \frac{\eta \beta_V P_V}{K} \\ 0 & 0 & 0 & 0 & 0 & -\mu_{FF} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -\mu_{FF} & 0 \\ 0 & 0 & 0 & 0 & \sigma_V & 0 & \sigma_{FF} & -\mu_E \end{pmatrix} \tag{34}$$

Let λ_i be the eigenvalues of J_{E_0}, for $i = 1,2,3,4,5,6,7,8$, the eigenvalues is computed as

$$\lambda_1 = -\mu_H < 0$$
$$\lambda_2 = -(\gamma + \mu_H) < 0$$
$$\lambda_3 = -(\theta + \mu_H) < 0$$
$$\lambda_4 = -\mu_V < 0$$
$$\lambda_5 = -\mu_{FF} < 0 \tag{35}$$
$$\lambda_6 = -\mu_{FF} < 0$$
$$\lambda_7 = -\frac{1}{2}\left(\mu_V + \mu_E - \sqrt{4\mu_V \mu_E R_0 + \mu_V^2 - 2\mu_V \mu_E + \mu_E^2} \right) < 0$$
$$\lambda_8 = -\frac{1}{2}\left(\mu_V + \mu_E + \sqrt{4\mu_V \mu_E R_0 + \mu_V^2 - 2\mu_V \mu_E + \mu_E^2} \right) < 0$$

From Equation (35), to show that λ_7 negative, we impose a negativity condition to it.

λ_7 is negative if and only if Equation (36) below holds

$$\sqrt{4\mu_V \mu_E R_0 + \mu_V^2 - 2\mu_V \mu_E + \mu_E^2} < (\mu_V + \mu_E) \tag{36}$$

Simplifying Equation (36), R_0 is obtained as Equation (37) below

$$R_0 < 1 \tag{37}$$

From Equation (37), it implies that λ_7 is negative.

Since the eigenvalues of J_{E_0} are all negatives it therefore shows that the disease-free equilibrium is locally asymptotically stable for $R_0 < 1$.

3.4. The Stability of the Endemic Equilibrium

The endemic equilibrium E_{ee} of the model is locally asymptotically stable if and only if $R_0 > 1$. However it is very difficult to deal with the stability of the endemic equilibrium analytically due to the nature of transmission model (i.e.

Model 3). By numerical approach, the endemic equilibrium is locally asymptotically stable. Different initial conditions were applied for the simulation. Those obits shown to be the same point as time evolve.
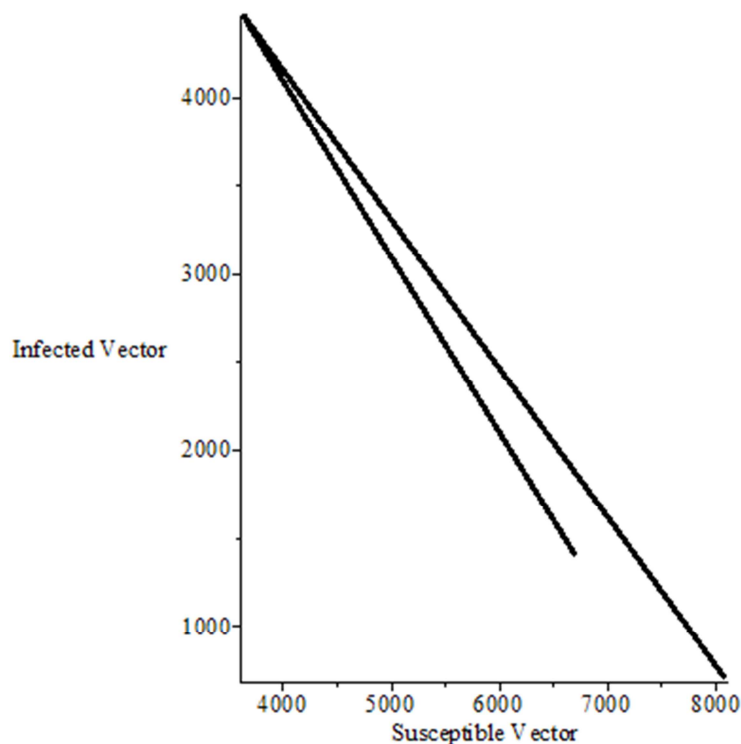

Figure 5. *Phase portrait of Model 3 in $S_V - I_V$ plane .*
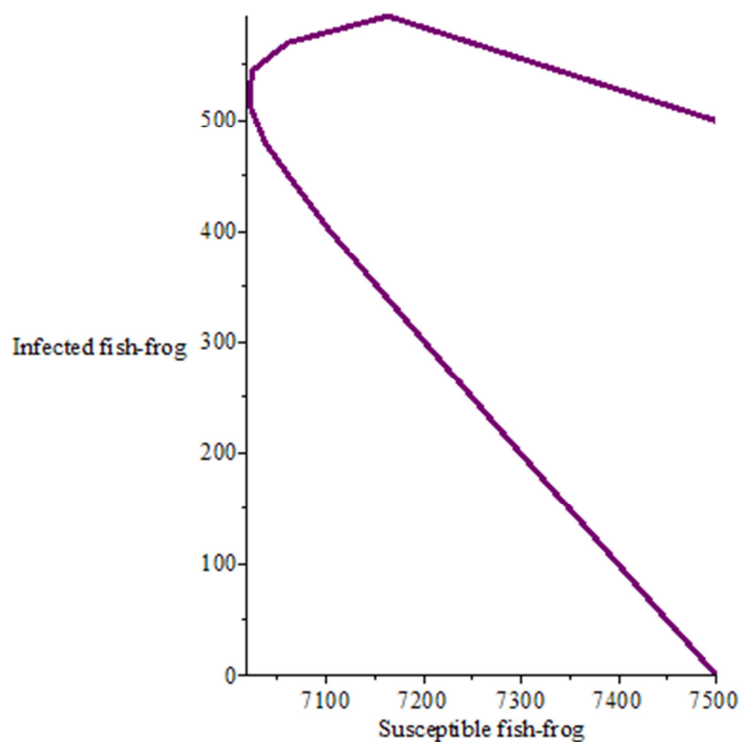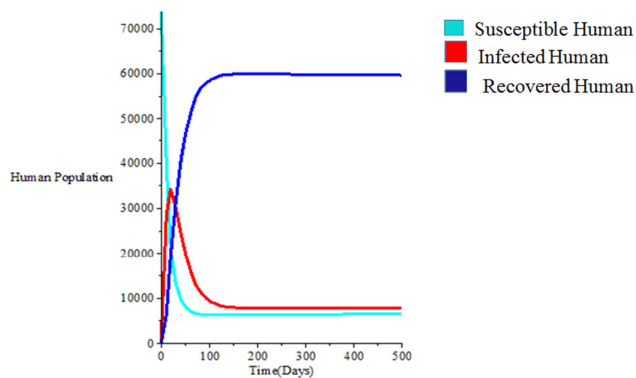
Figure 6. *Phase portrait of Model 3 in $S_{FF} - I_{FF}$ plane .*

Symbol	Description
β_H	The effective contact rate between the vector, fish-frog and susceptible human
β_V	The effective contact rate between fish-frog and susceptible vector
β_{FF}	The effective contact rate between the susceptible fish-frog and Mycobacterium Ulcerans
γ	The recovery rate of infected humans
θ	The rate of loss of immunity of recovered humans
μ_H	Birth rate of the human population
μ_V	Birth rate of the vector population
μ_{FF}	Birth rate of the fish-frog population
rV	The growth rate of the vector population
rF	The growth rate of the fish-frog population
K	The environmental carrying capacity of the bacteria population
σ_{FF}	Rate of shedding of Mycob acterium Ulcerans into the environment by fish-frog
σ_V	Rate of shedding of Mycobacterium Ulcerans into the environment by the vector
μ_E	Rate at which Mycobacterium Ulcerans are cleared from the environment.

Figure 7. Dynamics of Human compartment of Equation (3).

4. Results and Discussion

Numerical simulation of the Equation (3.6) was carried out using Maple inbuilt functions. Analysis of the response of model parameters on the transmission dynamics of the disease was studied and the evaluation of the basic reproduction number was made. Since, most of the parametric values are not readily available it is needed to assign some arbitrary values. However, some are available at [6, 11, 12]. The initial conditions were taken at initial time of zero (0) and the final time was considered as 500, 500, 500, 500, 520, 2000, 2000, 2000, 7000, 8000 and finally 10000. The results of the simulation study are presented in Figure 8.

From Figure 7 the model simulations show that the susceptible human population decrease and becomes steady with time. The infected human population also increases so sharply and becomes asymptotic with time. This is due to the rate at which a susceptible human is bitten by an infected water bug and also the rate at which a susceptible human feed on an infected fish-frog. It can be observed that the Recovered human population increases to a certain point and it then decreases asymptotically with time.
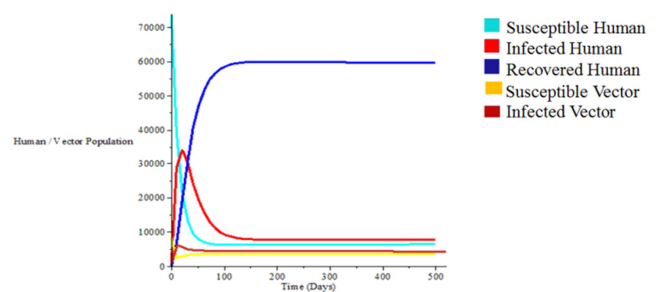

Figure 8. Dynamics of the Human and the Vector compartments.

Figure 8 shows the general interactions between human and vector population in the study areas with time. It's also shows that there will be a widespread occurrence of the Buruli Ulcer disease in study areas.

The basic reproduction number was calculated as

$$R_0 = 1.207710000$$

Equation Chapter (Next) Section 1 (38)

The positivity of solution to the model was proved as shown in Equation (4) to (17). The Basic Reproduction Number (R_0) was computed from the deterministic model that was developed in Equation (4). The model's equilibria were determined and conditions for the equilibria were also established, and their stabilities were investigated in terms of the classic threshold (R_0). It is well known in disease transmission modelling that, a classical necessary condition for minimizing or eliminating disease completely is that the basic reproduction number (R_0), must be less than unity. If the basic reproduction number is greater than unity, then the disease will eventually spread in a population. The disease-free equilibrium (DFE) is found to be locally asymptotically stable for $R_0 < 1$ as it's shown in Equation (37). The endemic equilibrium is also found to be locally asymptotically stable for $R_0 > 1$.

A simulation was performed on the model using some of the parameters in Table 3. The results obtained indicate that,

the disease has attained a steady state, this is typically shown in Figure 8. In examining the state of Buruli Ulcer in the study area, since $R_0 > 1$ it proves that the number of infected persons in the communities will increase with time.

5. Conclusions

The study developed a deterministic model for Buruli Ulcer based on the transmission mechanism of the disease in the study area. The basic reproduction number R_0 derived was found to be greater than unity (i.e. $R_0 > 1$), this shows that, the disease will spread horizontally across the population, and the estimated value of R_0 was 1.20771. The transmission dynamics of Buruli Ulcer model of the Susceptible, Infected and Recovered (SIR) type showed that, the disease will continue to spread at the study areas as long as the reservoir for Mycobacterium Ulcerans continue to increase and also as long as enough infected water bugs and infected fish or infected frog continue to increase. However, the spread of the disease (Buruli Ulcer) will be minimised when control measures are being implemented. It is therefore recommended that People in the affected communities should be given adequate education on the Buruli Ulcer disease, how contaminated water or stagnant water play a major role in the transmission of the disease and how the disease should be treated properly to minimize its spread.

Acknowledgements

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