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Mathematical and Sensitivity Analysis of Efficacy of Condom on the Transmission of Gonorrhea Disease

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Abstract: *Four (4) deterministic epidemiological model of (S, E, I, R) is studied to gain insight into the efficacy and compliance of condom on the dynamical spread of Gonorrhea disease. Positivity solution is analyzed for mathematical and epidemiological posedness of the model. Local and global stability of the model are explored for disease-free and endemic equilibria. Sensitivity analysis is performed on the basic reproduction number to check the importance of each parameter on the transmission of gonorrhea disease. Numerical simulation is analyzed by MAPLE 18 software using embedded Runge-Kutta method of order (4) which shows the effect of condom on the prevention/control of Gonorrhea disease.*

Keywords: *Gonorrhea, Condom, Reproduction number, Stability, Next generation matrix, Sensitivity, Critical points.*

1. Introduction

Gonorrhea is one of the sexually lethal transmitted diseases (STD), due to the number of complications that it causes in the infected persons [18]. The disease is caused by Neisseria Gonorrhea, a bacterium. Gonorrhea is formed in the warm, moist area of the reproductive tract such as the cervix, uterus and the fallopian tubes in women and in the urethra in both women and men [9]. The history of Gonorrhea goes down to 1792, in Edinburg where the surgeon Benjamin Bell clearly differentiated it from syphilis infection [5]. Gonorrhea has a lot of complications in the infected persons, and a prolong infection can lead to severe eye infections, infertility in both men and woman, ectopic pregnancy, spontaneous abortion, still births and eventually death if untreated [13]. In 1970 gonorrhea led the list of infectious diseases in the number of cases reported to the U.S. Public Health Service, with more cases than the combined total for syphilis, mumps, measles, German measles, and infectious hepatitis [2].

(WHO, 2012) [26], estimated approximately 106 million new cases of gonorrhea among adults globally. This is just an embodiment of the reported cases from Gonorrhea bacterium infection in that year. Gonorrhea is in essence a non-seasonal disease with less than a 10 percent seasonal component in the variation [8], the average incubation period is short, 3 to 10 days, compared to the often quite long period of active infectiousness. An infected individual seems to remain infectious until he or she receives antibiotic treatment. While some infected individuals (especially men) quickly develop painful symptoms and therefore seek prompt medical treatment, others do not. It has long been recognized that infected women may have no easily recognizable symptoms [15], even while the disease does substantial internal damage. A study [14] of servicemen demonstrated that men also can be infected without symptoms. Some studies indicate that a substantial fraction of the men in the studies who became infected through contacts with infected opposite sex had no symptoms [4].

The bacterium also grows in the mouth, throat, eyes and anus [12]. First noticeable signs from the infection in men are often a painful sensation during urination, persistent sore throat and pains in the testicles. Women however don't develop overt signs of the disease. When women have the symptoms, they tend to be mild or similar to other infections, making them more difficult to identify. Some of the symptoms women experience are discharge from the vagina, frequent urination, sore throat and uneasy sensation while urinating [6]. Gonorrhea transmission happens through direct contact with exudates from mucous membranes of infected people through unprotected oral, anal or vaginal sex. Infected people without the symptoms are likely to spread the infection to others if

condoms and dental dams are not used during sexual intercourse [19].

It was proved that the disease will die out either for all positive initial disease levels or for none, depending on the contact rates and the lengths of infectious periods, they also proved that if the initial number of infectives in at least one group is not zero, then the disease will remain endemic and the number of infectives in each group will approach a constant positive level. This behavior of gonorrhea epidemics is different from most other infectious diseases, which usually have occasional major outbreaks followed by low disease levels. This different behavior of gonorrhea is attributable to the lack of developed immunity and the basic non-seasonality of the disease [2]. Gonorrhea treatment can be achieved through a positive rapid diagnostics and nuclei test, followed by the administration of antibiotics in adolescents and adults [27]. However, a drug-resistant strains of the bacterium has recently awakened public health bodies on the area of finding an alternative drugs for the treatment of the disease [17].

A mathematical model specifically for gonorrhea was first developed by Cooke and Yorke [7]. They considered a single homogeneous population, using time delays to represent variation in the infectious period. The difficulty of analyzing differential equations with time delays makes it unlikely that their approach can be extended to general non-homogeneous population with varying contact rates. The model [2] developed uses a system of ordinary differential equations without time delays. Gonorrhea case reports are at present increasing, at least in part because of changing social and medical factors and have no way to estimate the magnitude or even directions of all these changes, so modeling of [2] was restricted to constant epidemiological factors, allowing changes only in the case rates as a result of population interactions.

Since discovered, numerous imperative works have been contributed by mathematical and non-mathematical researchers, and these works have helped immensely in the area of vaccine development and control intervention strategy to vaccine manufacturers and public health workers at large. Garnett et al [11], examined the sexual behavior of gonorrhea patients in New York, and used it to estimate the parameters of their gonorrhea model. Their model was used to assess the potential impacts of treatment intervention. Kretzschmar et al [20], proposed a stochastic model for gonorrhea which analyze the underlying structure of sexual contact pattern. They compared the benefits of condom use in an age-structured population of sexually active core group. Prabhakararao [24], analyzed a mathematical model of Gonorrhea disease. They ascertained that the spread of the disease involves interaction of the susceptible and the infective. Leung and Gopalsamy [23], formulated a continuous time SIV model for Gonorrhea transmission among homosexuals. They also used a non-standard discretization method to formulate a discrete time model, and they compared the results of their models. Yorke [21],modelled the spread of Gonorrhea in a population that was categorized into n group and used it to further study the asymptotic stability of the model. Kishore and Pattabhiramacharyulu [25], proposed a simple non-linear first order ODE model for Gonorrhea that measure the growth rates of promiscuous and infective in a homosexual population. They further used numerical examples to explain the effect of cure rate and infective rate on the spread and control of the disease. Adesanya et al [1], also used non-linear differential mathematical equations to studied effect of chemoprophylaxis treatment on the dynamical spread of gonorrhea. Their results showed that early treatment of the disease greatly reduced the dynamical spread of the disease in the community.

Besides the mathematical models, an equally outstanding contribution has been achieved by the non-mathematical models. Karnath [16], discusses the symptoms and signs of Neisseria Gonorrhea with regards to the genitourinary and extra-genital, and outlines laboratory diagnosis with recommended treatment measures. Benedek [5], discusses the unsuccessfulness of various experiments in an attempt to infect animals with Gonorrhea infection as well as history of researches on causes and spread of Gonorrhea in humans over the decades. Bala [3], compared and compiled the resistance trends of Neisseria Gonorrhea across various countries of south-East Asia Region by means of surveillance.

In this research work, compliance and efficacy of condom were used as control measures to reduce the basic reproduction number of the disease. Since dynamical transmission of the gonorrhea disease is dependent on the value of basic reproduction number R_0.

2. Mathematical model

We considered four (4) compartmental deterministic mathematical model using the S, E, I, Rto have better understanding of efficacy and compliance of condom on Gonorrhea disease. The population size $N(t)$ is sub–divided into sub–classes of individuals who are Susceptible $S(t)$, Exposed E (t), Infected $I(t)$, and Recovered $R(t)$, where

$$N(t) = S(t) + E(t) + I(t) + R(t) \qquad (1)$$

Susceptible (S): Susceptible individual is a member of a population who is at risk of becoming infected by a disease. The population of susceptible individuals increases by the recruitment of sexually-active individuals at a rate π. The population decreased by natural death at a rate μ also, by infection following a contact with infected individuals who did not use condom at a rate β. The susceptible population later increased by recovered individuals after the wanes of treatment (γ).

Exposed (E): Exposed individual is a member of a population who is infected but not infectious. The population of exposed individuals increases through the infection of susceptible and are assumed to show no disease symptoms initially. The population of exposed class diminished by the progression of exposed individual to infected class I at a rate (σ) and by natural death at a rate μ.

Infected (I): Infected individual is a member of a population who is infected and capable of transmitting the disease. The population of infected individuals is increased following the progression of exposed individual at a rate (σ). The population is decreased by natural death, disease induced death and treatment at the rate (μ), (δ) and (τ) respectively

Recovered (R): Recovered individual is a member of a population who recovered from the disease. The population of recovered individual is increased by the treatment of infected individual at a rate (τ), this population later decreased by natural death and individuals that loss immunity since there is no permanent immunity to gonorrhea at the rate (μ and γ).

Hence, we have the following non linear system of differential equations:

$$\left.\begin{aligned}
\frac{dS}{dt} &= \pi - (1-\upsilon\phi)\beta S(t)I(t) - \mu S(t) + \gamma R(t)\\
\frac{dE}{dt} &= (1-\upsilon\phi)\beta S(t)I(t) - (\sigma+\mu)E(t)\\
\frac{dI}{dt} &= \sigma E(t) - (\mu+\delta+\tau_1)I(t)\\
\frac{dR}{dt} &= \tau_1 I(t) - (\mu+\gamma)R(t)
\end{aligned}\right\} \quad (2)$$

2.1. Positivity of Solution

Lemma 1

The closed set $D = \{(S+E+I+R) \in R^4_+ : N \le \pi/\mu\}$ is positively-invariant and attracting with respect to the model in (2)

Proof: Consider the biologically-feasible region D, defined above. The rate of change of the total population, obtained by adding all equations of the model in (2), is given by

$$\frac{dN}{dt} = \pi - \mu N - \delta \quad (3)$$

It follows that $\frac{dN}{dt} < 0$ whenever $N > \frac{\pi}{\mu}$.

Furthermore,

Since $\frac{dN}{dt} \le \pi - \mu N$, it is clear that $N(t) \le \frac{\pi}{\mu}$

if $N(0) \le \frac{\pi}{\mu}$.

Therefore, all solutions of the model with initial conditions in D remain in D for all $t > 0$ (i.e., the ω-limits sets of the system in (2) are contained in D). Thus, D is positively-invariant and attracting. In this region, the model can be considered as been epidemiologically and mathematically well posed

2.2. Disease Free Equilibrium

For critical points, we set;

$$\frac{dS}{dt} = \frac{dE}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = 0 \quad (4)$$

At disease free equilibrium, we assumed there is no infection in the population.

Let ε_0 denotes the disease free equilibrium. Thus;

The model in (2) has disease free equilibrium given by

$$\varepsilon_0 = (S,E,I,R) = \left(\frac{\pi}{\mu},0,0,0\right) \quad (5)$$

2.3. Endemic Equilibrium

The endemic equilibrium of the model (2) is given below;

$$\left.\begin{aligned} S^* &= \frac{K_1 K_2}{\beta\sigma(\upsilon\phi+1)} \\ E^* &= \frac{K_2 K_3 A}{\beta\sigma B} \\ I^* &= \frac{K_3 A}{\beta B} \\ R^* &= \frac{\tau A}{\beta B} \end{aligned}\right\} \quad (6)$$

Where

$$A = (\sigma\upsilon\phi\pi\beta - \mu K_1 K_2 + \sigma\pi\beta)$$

$$B = (\sigma\upsilon\tau\phi\gamma - \upsilon\phi K_1 K_2 K_3 - \tau\gamma\sigma + K_1 K_2 K_3)$$

$$K_1 = \mu + \sigma$$

$$K_2 = \mu + \delta + \tau$$

$$K_3 = \mu + \gamma$$

Using next generation matrix [10], the non-negative matrix F (new infection terms) and non-singular matrix V (other transferring terms) of the model are given, respectively by;

$$F = \begin{pmatrix} (1-\upsilon\phi)\beta SI \\ 0 \\ 0 \end{pmatrix}, V = \begin{pmatrix} (\mu+\sigma)E \\ -\sigma E + (\mu+\delta+\tau)I \\ -\tau I + (\mu+\gamma)R \end{pmatrix} \quad (7)$$

After taking partial derivatives of F and V, we have:

$$F = \begin{pmatrix} 0 & \frac{(1-\upsilon\phi)\beta\pi}{\mu} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \quad (8)$$

$$V = \begin{pmatrix} (\mu+\sigma) & 0 & 0 \\ -\sigma & (\mu+\delta+\tau) & 0 \\ -\tau & 0 & (\mu+\gamma) \end{pmatrix} \quad (9)$$

Thus;

$$R_0 = \frac{(1-\phi\upsilon)\beta\pi\sigma}{\mu(\mu^2 + \mu\tau + \mu\delta + \mu\sigma + \tau\sigma + \delta\sigma)}$$

The threshold quantity R_0 is the basic reproduction number of the normalized model system (2) for Gonorrhea infection. It is the average number of new secondary infections generated by a single infected individual in his or her infectious period. [1].

3. Local Stability

Theorem 1: The disease free equilibrium of the modeled in equation (2) is locally asymptotically stable (LAS) if $R_0 < 1$ and unstable if $R_0 > 1$.

Proof: To determine the local stability of E_0, the following Jacobian matrix is computed corresponding to equilibrium point E_0. Considering the stability of the disease free equilibrium at the critical point $\left(\frac{\pi}{\mu}, 0, 0, 0\right)$.

We have

$$J_G = \begin{pmatrix} -\mu-\lambda & 0 & \frac{-\beta(1-\upsilon\phi)\pi}{\mu} & \gamma \\ 0 & -(\sigma+\mu)-\lambda & \frac{\beta(1-\upsilon\phi)\pi}{\mu} & 0 \\ 0 & \sigma & -(\mu+\delta+\tau)-\lambda & 0 \\ 0 & 0 & \tau & -(\mu+\gamma)-\lambda \end{pmatrix}$$

The eigen values are $\lambda = -\mu$ and $-(\mu+\gamma)$ and the remaining matrix J_G is given by;

$$J_G = \begin{vmatrix} -(\sigma+\mu)-\lambda & \frac{\beta(1-\upsilon\phi)\pi}{\mu} \\ \sigma & -(\mu+\delta+\tau)-\lambda \end{vmatrix} = 0$$

(10)

The characteristics polynomial of (10) is given by

$$B_2\lambda^2 + B_1\lambda + B_0 = 0 \quad (11)$$

Where

$$B_2 = 1$$

$$B_1 = (2\mu + \delta + \tau + \sigma)$$

$$B_0 = \frac{-(1-\phi\upsilon)\beta\pi\sigma}{\mu} + (\mu^2 + \mu\tau + \mu\delta + \mu\sigma + \tau\sigma + \delta\sigma)$$

$$B_0 = \frac{(1-\phi\upsilon)\beta\pi\sigma}{\mu(\mu^2 + \mu\tau + \mu\delta + \mu\sigma + \tau\sigma + \delta\sigma)} < 1$$

Hence

$$R_0 < 1$$

(12)

Then according to Routh Hurwitz criterion all the roots of the polynomial will have negative real

parts if and only if all the coefficients B_i (i=0, 1, 2) are all positive and that the matrices T_i (i=1, 2) are all positive. From (12) above $B_2 > 0, B_1 > 0$ and $B_0 > 0$ if $R_0 < 1$. Also, the Hurwitz matrix are given below;

$$T_1 = B_1 > 0,\ T_2 = \begin{vmatrix} B_2 & 1 \\ 0 & B_0 \end{vmatrix} > 0,$$

The result from Routh Hurwitz criterion shows that, all eigen values of the polynomial are negative which shows that the disease free equilibrium is locally asymptotically stable.

4. Global Stability

Theorem 2: The disease free-equilibrium of the system in (2) is globally asymptotically stable whenever $R_0 < 1$ and unstable if $R_0 > 1$.

Proof: It follows that $S = N^* - E - I - R$ at steady state.The proof is based on using the comparison theorem [18]. The rate of change of the variables representing the infected component of the system can be written as follows.

$$\left.\begin{aligned} \frac{dE}{dt} &= (1-\upsilon\phi)\beta I(N^* - E - I - R) - (\mu+\sigma)E \\ \frac{dI}{dt} &= -\sigma E - (\mu+\delta+\tau)I \\ \frac{dR}{dt} &= \tau I - (\mu+\gamma)R \end{aligned}\right\} \quad (13)$$

For the model in (2), the associated reproduction number is denoted by R_0, where

$$R_0 = \frac{(1-\phi\upsilon)\beta\pi\sigma}{\mu(\mu^2 + \mu\tau + \mu\delta + \mu\sigma + \tau\sigma + \delta\sigma)}$$

The DFE of the model (5) is GAS in D^* if $R_0 < 1$.
Using comparison method, we have,

$$\begin{pmatrix} \frac{dE}{dt} \\ \frac{dI}{dt} \\ \frac{dR}{dt} \end{pmatrix} = (F-V)\begin{pmatrix} E \\ I \\ R \end{pmatrix} - Fi\begin{pmatrix} E \\ I \\ R \end{pmatrix} \quad (14)$$

Then

$$\begin{pmatrix} \frac{dE}{dt} \\ \frac{dI}{dt} \\ \frac{dR}{dt} \end{pmatrix} \le (F-V)\begin{pmatrix} E \\ I \\ R \end{pmatrix} \quad (15)$$

According to [10], all eigenvalues of the matrix F – V have negative real parts. It follows that the linearized differential inequality above is stable whenever $R_0 < 1$.Consequently $S = (E = I = R = 0) \to (0, 0, 0)\ at\ t \to \infty$ .Substituting $E = I = R = 0$ in (R_0) gives $S(t) \to S(0)\ as\ t \to \infty$. Hence, we have established that the disease free equilibrium is globally asymptotically stable whenever $R_0 < 1$.

5. Sensitivity Analysis

Sensitivity analysis is a crucial analysis that shows importance of each parameter to disease transmission. The sensitivity index of parameters with respect to the basic reproduction number is calculated, to know how crucial each parameter is to the disease transmission; intervention control strategies that target such parameter should be employed in the control/prevention of gonorrhea disease.

Definition 1. The normalized forward sensitivity index of a variable ω that depends differentiably on a parameter p is defined as:

$$X_P^{\omega} = \frac{\partial\omega}{\partial P} \times \frac{P}{\omega}. \quad (16)$$

As we have explicit formula for R_o, we derive an analytical expression for the sensitivity of R_o as

$$X_P^{R_o} = \frac{dR_o}{dP} \times \frac{P}{R_o}$$

The signs of the sensitivity index of R_0 are as shown in the table 3.

6. Numerical Simulation

Numerical simulation was carried out by MAPLE 18 software using Runge-Kutta method of order four with the set of parameter values given in table 4. Condom efficacy and compliance is checked simultaneously on Susceptible, Exposed and Infected individuals since efficacy of condom is a function of compliance of condom.

Figures 1-3 below are the results obtained from numerical simulation of the Gonorrhea model with condom efficacy/compliance.

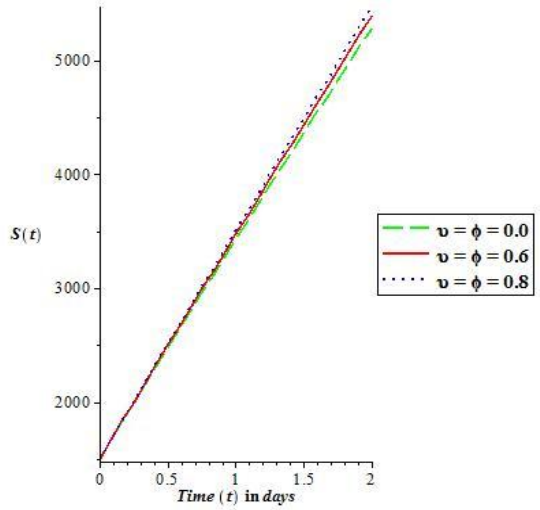

*Fig.*1 *Graph of Susceptible individuals for Various Values of condom efficacy and compliance*

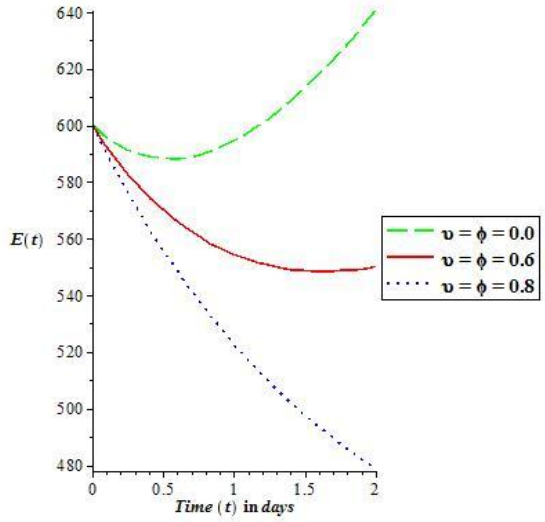

*Fig.*2 *Graph of Exposed individuals for Various Values of condom efficacy and compliance*

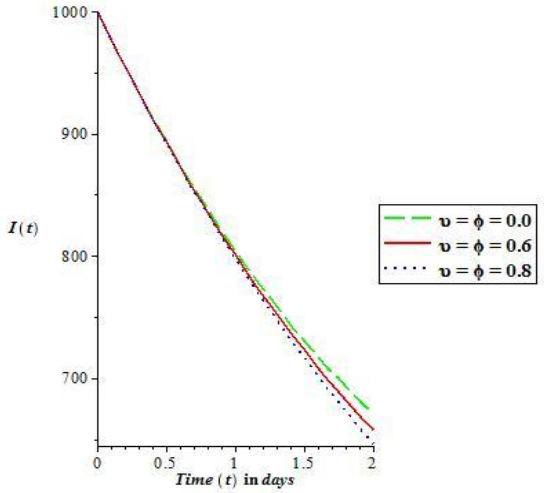

*Fig.*3 *Graph of Infected individuals for Various Values of condom efficacy and compliance*

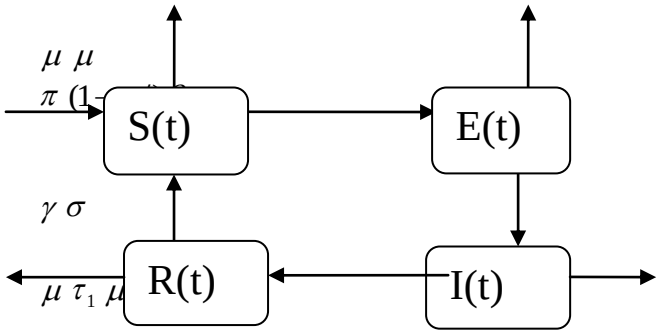

Figure 1. Flow Chat

Table 1. Description of Variables

Variables	Definitions
S	Susceptible individuals
E	Exposed individual
I	Infected individual
R	Recovered individual

Table 2. Description of Parameters

Parameters	Definitions
τ	Treatment rate
υ	Efficacy of condom.
ϕ	Compliance of condom
π	Recruitment rate
μ	Natural death rate
σ	Progression rate
γ	Loss of immunity
δ	Induced mortality rate

β	Effective contact rate
N	Total population

Table 3. Signs of Sensitivity Index of R_0

Parameter	Sensitivity Index
τ	Negative
υ	Negative
ϕ	Negative
π	Positive
μ	Negative
σ	Positive
δ	Negative
β	Positive

Table 4. The Numerical Values of Parameters

Parameter	Value
τ	0.6
υ	0.7
ϕ	0.5
π	2000
μ	0.01
σ	0.6
δ	0.03
β	0.1

7. Results and Discussions

In this study, Four (4) deterministic epidemiological model of (S, E, I, R) are presented to gain insight into the compliance and efficacy of condom on the dynamical spread of Gonorrhea disease. Positivity of solution shows that, the model presented is mathematically and epidemiologically well posed. Local and global stability of the model shows that, disease-free equilibrium is asymptotically stable whenever the threshold quantity 'R_0' is less than unity and otherwise endemic when it is greater than unity. Sensitivity analysis of the model shows that increase or decrease in the value of each parameter with negative sign in basic reproduction number 'R_0' can increase or decrease 'R_0'. **Figures 1-3** of numerical simulation showed that, increasing the rate of efficacy/compliance of condom reduces the exposed and infected individuals.

In conclusion, the use of condom with total compliance can reduce the spread of Gonorrhea disease. Increment in the values of condom efficacy/compliance reduced the basic reproduction number 'R_0' since the spread of disease is dependent on the value of 'R_0'. Therefore effort that targets the use of condom as a control measure should be encouraged.

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