Quest for Research Excellence On Computing, Mathematics and Statistics

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Faculty of Computer and Mathematical Sciences

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Chapters in Book

The 2nd International Conference on Computing, Mathematics and Statistics (iCMS2015)

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Content

CHAPTER 16
Sensitivity Index of HIV-1 model Parameters with Vertical transmission

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Abstract. A non-linear deterministic mathematical model is considered to study the dynamics of HIV-1 with vertical transmission. The total population is divided into four mutually exclusive classes of susceptible, asymptomatic, symptomatic and AIDS individuals. Invariant region and positivity solution of the model is determined. The model threshold parameter is investigated using next generation operator method. Sensitivity analysis of the model parameters was carried out in order to identify the most sensitive parameters on the disease transmission. The results indicate that, the most sensitive parameters are the contact rate of the susceptible human with the asymptomatic individuals (β_2). The next is the number of sexual cohort of the susceptible individuals with the asymptomatic individuals (c_2). The least sensitive parameter is the fraction of susceptible newborn from infectives class (ε)

Keywords: HIV/AIDS; sensitivity index; vertical transmission; basic reproduction number.

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1 Introduction

Several infectious diseases in nature spread through both horizontal and vertical ways. These diseases include HIV/AIDS, Chagas, rubella etc, [1]. Horizontal transmission usually occurs through direct or indirect bodily contact with infectious hosts. Vertical transmission takes place from an infected mother to its newborn, before, during, after delivery or during breast feeding [2]. Other ways for HIV/AIDS transmission include, use of unsterilized needles for intravenous drugs users. Since the beginning of the HIV-1 (human immunodeficiency syndrome sub- type 1) epidemic in 1981 to date, nearly more than 78 million people have been infected with the virus. Majority of them reside in sub-Saharan Africa. And nearly 39 million people have died of AIDS related complications [3]. Globally, about 1.5 million pregnant women were living with HIV, but more than 90% are found in sub-Saharan Africa. Research has shown that more than 1000 new cases of newborn infected with HIV-1 were recorded every day as at 2012 [4]

Vertical transmission (mother to child), of HIV/AIDS is one of the major contributors to the extreme child and infant mortality especially in sub-Saharan Africa. One third of infected infants are projected to die before they had their first birth day [5]. While more than half will die before their second birthday as such, their life expectancy is extremely short [6]. But studies have shown that some HIV-positive mothers gave birth to the HIV-negative babies [7]. As a result of that, this work considers HIV negative babies born by the infected mothers in the upcoming model formulation. Any pregnant woman tested positive with HIV, medication supposed to begin immediately, and continue throughout the pregnancy period, during labor and post natal period when the baby is exclusively breastfed. Hence, this medication is an intervention to prevent the transmission of the virus from infected mothers to their newborn (PMTCT). The intervention decline the risk of mother to child transmission to less than 1% [8].

Mathematical models for long have been largely used into the epidemiology of HIV, to advance our understanding of the major causative factors in a given epidemic. From the first model of the virus by May and Anderson in 1986 [9], various improvements have been added into modeling outlines, see for instance, [10, 11]. Modeling the spread of HIV with vertical transmission has received great effort. [12] formulated a model of mother to child transmission, where by the infected mothers directly increase the population of infected classes. They emphasize that, in order to keep the overall infective population under control, use of condom and other effective treatment has to be considered. [13] Extended the work of [12], by incorporating treatment, the analysis of the model has shown that, using treatment as an intervention on controlling the vertical transmission has great effect on reducing the transmission of the virus. [14] formulated an HIV/AIDS

model with vertical transmission and infected immigrant, basic properties of the model investigated, analysis of the model revealed that an increase in the vertical transmission in the population lead to the increase in the population of infective.

Therefore, this study aimed at developing a deterministic mathematical model of HIV/AIDS with vertical transmission (mother to child). The study also investigates the role of each parameter on the disease transmission. This is done by considering the four stages of HIV/AIDS infection by joint united nation programmed on HIV/AIDS (UNAIDS). This will guide the policy makers and health practitioners on the key parameters to be considered on the virus spread. The paper is organized as follows: Section 2 contains the model assumption and formulation. In section 3, some basic properties of the model investigated. Section 4, sensitivity analysis is carried out to obtain the strength of each parameter on the virus transmission. In section 5, numerical simulation is presented and lastly, conclusion is contained in section 6.

2 Model Formulation

The model sub-divides the total human population at a time *t*, denoted by $N_h(t)$, into the following sub populations of susceptible human $S(t)$, asymptomatic individuals $\left(I_1(t)\right)$ (infected individuals with no symptoms of infection), symptomatic individuals $\left(I_2(t)\right)$ (infected individuals with symptoms of infection) and lastly the AIDS patients $A(t)$. Thus;

$$N(t) = S(t) + I_1(t) + I_2(t) + A(t) \tag{2.1}$$

The model assumed that humans are born susceptible (without infection), at a rate Q_0. It is also assumed that some infected mothers gave birth to a newborn without infection which added to the susceptible class, at a rate $z\varepsilon$, as z is the birth rate and ε is the fraction of susceptible newborn. Susceptible human are reduced as a result of infection through sexual contact with the asymptomatic individuals at a rate $\beta_1 c_1 I_1$. The contact rate is given by β_1 while c_1 is the average number of sexual partners. The population is also reduce through sexual contact with the symptomatic individuals at a rate $\beta_2 c_2 I_2$, β_2 is the contact rate and c_2 is the average number of sexual partners. The total population suffers a natural death at a rate μ. Asymptomatic class increased as a result of infection by the susceptible

individuals and also through birth of infected mothers at a rate $(1-\varepsilon)$, as $(1-\varepsilon)$ is the remaining fraction for the infected newborn. The class is reduced through developments of symptoms of infection at a rate α which added to the symptomatic class. The class is reduced through development of full blown AIDS at a rate κ. Thus; it added to the AIDS class, the AIDS class suffers additional death modulus due to infection at a rate σ.

Therefore, putting the above assumptions and formulations the following system of ordinary differential equations is obtained as follows;

$$\left.\begin{aligned}
\frac{dS}{dt} &= Q_0 + z\varepsilon\left(I_1 + I_2\right) - \beta_1 c_1 I_1 S - \beta_2 c_2 I_2 S - \mu S \\
\frac{dI}{dt} &= \beta_1 c_1 I_1 S + \beta_2 c_2 I_2 S + z\left(1-\varepsilon\right)\left(I_1 + I_2\right) - \left(\mu + \alpha\right) I_1 \\
\frac{dI_2}{dt} &= \alpha I_1 - \left(\mu + \kappa\right) I_2 \\
\frac{dA}{dt} &= \kappa I_2 - \left(\mu + \sigma\right) A
\end{aligned}\right\} \qquad 2.2$$

Table 1 and 2, below described the variables and parameters used in the model,

Table 1.1; Description of variables of HIV/AIDS model

Variables	Description
S	Susceptible human
I_1	Asymptomatic human
I_2	Symptomatic human
A	AIDS human

3 Basic Properties of the HIV/AIDS model

3.1 Invariant Region;

Let the set, $\Omega = \left\{ \left(S, I_1, I_2, A\right) \in \mathbb{R}_+^4 : N \le \frac{Q_0}{\mu} \right\}$

Be the region of interest biologically, this is positively invariant under the flow induced by the model equation (2.6). Hence, the model system (2.6) can be rewritten in the following Metzler system;

$$\frac{dX}{dt} = M(\mathrm{X})\,\mathrm{X} + \mathrm{F} \qquad 2.3$$

When

$$X = \left(S, I_1, I_2, A\right), \lambda_1 = \beta_1 c_1 I_1, \lambda_2 = \beta_2 c_1 I_2, \omega = z\left(1-\varepsilon\right), \tau = z\varepsilon$$

$$M(\mathrm{X}) = \begin{pmatrix} -\left(\lambda_1 + \lambda_2 + \mu\right) & \tau & \tau & 0 \\ \left(\lambda_1 + \lambda_2\right) & -\left(\mu + \alpha\right) + \omega & \omega & 0 \\ 0 & \alpha & -\left(\mu + \kappa\right) & 0 \\ 0 & 0 & \kappa & -\left(\mu + \sigma\right) \end{pmatrix}$$

And $F = \left(Q_0, 0, 0, 0\right)^T$. Since $M(\mathrm{X})$ have all off-diagonal entries nonnegative, therefore $M(\mathrm{X})$ is a Metzler matrix. Hence for $F \ge 0$ system (2.6) is positively invariant in $\mathbb{R}_+^4$ [18]

3.2 Positivity of solution

Lemma 1.1; Let the initial data be;

$\left\{ S(0) > 0, \left(I_1(0), I_2(0), A(0)\right) \ge 0 \right\} \in \Omega$, then, the solution set $\left\{S, I_1, I_2, A\right\}(t)$ of the model system (2.6) is positive for all $t > 0$.

Proof; from model system (2.6) the first equation gives**,**

$$\left.\begin{aligned}
&\frac{dS}{dt} = Q_0 + z\varepsilon\left(I_1 + I_2\right) - \left(\lambda_1 + \lambda_2 + \mu\right)S \geq -\left(\lambda_1 + \lambda_2 + \mu\right)S \\
&\frac{dS}{dt} \geq -\left(\lambda_1 + \lambda_2 + \mu\right)S \\
&\int \frac{dS}{S} \geq -\int \left(\lambda_1 + \lambda_2 + \mu\right)dt \\
&S\left(t\right) \geq S\left(0\right)e^{-\left(\lambda_1 + \lambda_2 + \mu\right)t} \\
&S\left(t\right) \geq 0
\end{aligned}\right\} \qquad 2.4$$

Equally, it can be shown that, $I_1\left(t\right), I_2\left(t\right), A\left(t\right) > 0$ for all $t > 0$, this complete the proof [11, 12]

3.3 Disease free equilibrium

In order to obtain the disease free equilibrium of the model system (2.6) the right-hand sides of the model equations is set to zero, hence, it give's,

$$\left.\begin{aligned}
&Q_0 + z\varepsilon\left(I_1 + I_2\right) - \beta_1 c_1 I_1 S - \beta_2 c_2 I_2 S - \mu S = 0 \\
&\beta_1 c_1 I_1 S + \beta_2 c_2 I_2 S + z\left(1-\varepsilon\right)\left(I_1 + I_2\right) - \left(\mu + \alpha\right)I_1 = 0 \\
&\alpha I_1 - \left(\mu + \kappa\right)I_2 = 0 \\
&\kappa I_2 - \left(\mu + \sigma\right)A = 0
\end{aligned}\right\} \qquad 2.5$$

The disease-free equilibrium points (DFE) are equilibrium-state solutions where there is no disease (HIV/AIDS). The diseased classes are equal to zero. Thus, the (DFE) of the basic model (2.6) is given by,

$$E^* = \left(\frac{Q_0}{\mu}, 0, 0, 0\right) \qquad 2.6$$

This symbolizes the state where there exists no infection in a community and it is acknowledged as the disease-free equilibrium point (DFE) [12, 13].

Table 1.2; Description of parameters of HIV/AIDS model

parameter	Description	Est. value	Ref
Q_0	Recruitment rate of human	0.029	[17]
z	Birth rate of infective newborn	0.03	Assumed
ε	Fraction of susceptible newborn from infective class	0.4	Assumed
β_1	Contact rate of susceptible with asymptomatic infective	0.2	[15]
β_2	Contact rate of susceptible with symptomatic infective	0.08	[15]
c_1	Number of sexual partners of susceptible with asymptomatic infective	2.0	Assumed
c_2	Number of sexual partners of susceptible with symptomatic infective	2.0	[16]
μ	Natural death rate	0.02	[16]
α	Removal rate to symptomatic class	0.6	[16]
κ	Rate of development to AIDS	0.1	[16]
σ	AIDS related death rate	1.0	[16]

4 Basic Reproduction Number

The Basic reproduction number $(\Re_0)$ is defined as the average number of fresh cases of an infection caused by one distinctive diseased individual in a population consisting of susceptible individuals only [19]. It is perhaps the most important measure in infectious disease epidemiology as it provides understandings into the disease dynamic forces and can propose appropriate control strategies. The parameter is computed using the next- generation approach [20]. Let the appearance of new infection in a compartment be F_i while V_i is the transfer of individuals out of compartment by any other means. Let E^* be the infection – free equilibrium, Hence, the associated basic reproduction number is given by,

$$\Re_0 = \frac{z(1-\varepsilon)\mu^2 + \beta_1 c_1 Q_0(\mu-\kappa) + \beta_2 c_2 \alpha Q_0 + (1-\varepsilon)(\kappa+\alpha)z\mu}{\mu(\mu+\kappa)(\mu+\alpha)} \quad 2.7$$

Moreover, using Theorem 2 of [20] the following result is established.

Theorem 1.0 The DFE of the model (2.6), given by (2.10) is locally asymptotically stable (LAS) if $\Re_0 < 1$ and unstable if $\Re_0 > 1$.

5 Sensitivity Analysis of Model Parameters

Sensitivity of each parameter is observed with respect to the basic reproduction number $\Re_0$. In this way, the parameters that are more sensitive to the virus transmission are known. And by either decreasing or increasing such parameters will as well decrease or upsurge the transmission of the virus. Sensitivity index of the basic reproduction number, $\Re_0$ with respect to each parameter is computed for the model equation (2.6).

5.1 Sensitivity indices of $\Re_0$

The Sensitivity of $\Re_0$ to each of the (10) diverse parameters described in table 1.3 are determined using basic reproduction number of the basic model (2.6) stated below,

Table 1.3 Sensitivity Indices of $\Re_0$

parameter	value	Sensitivity index
β_2	0.08	+1.6277
c_2	2.0	+0.6177
κ	0.1	-0.5637
β_1	0.2	+0.3140
c_1	2.0	+0.3138
Q_0	0.029	+0.3214
α	0.6	-0.2913
μ	0.02	-0.0866
z	0.03	+0.0584
ε	0.4	-0.0389

Table 1.3, above consists of parameter values for the sensitivity analysis that are arranged in order of magnitude. The most sensitive parameters include the contact rate of susceptible human with the symptomatic individuals β_2. The next important parameter in virus transmission is the number of sexual partners of susceptible with the asymptomatic individuals c_2. Other important parameters include the rate of development to AIDS by the asymptomatic individuals κ. Followed, by the contact rate of susceptible individuals with the asymptomatic individuals, while the least sensitive parameter, is the fraction of susceptible newborn from infective class ε. The sensitivity index of $\Re_0$ with respect to the contact rate of susceptible with the asymptomatic humans (β_2) is +1.6277 that means, increasing (or decreasing) the β_2 by 10%, increases (or decreases) $\Re_0$ by 16%. The sensitivity index of number of sexual cohorts of susceptible with the symptomatic human (c_2) is +0.6177, this implies that increasing (or decreasing) the c_2 by 10% increases (or decreases) $\Re_0$ by 6.2%. However, reducing the contact rate of susceptible humans with both the asymptomatic and symptomatic individuals through reducing the number of sexual cohorts will definitely reduce the spread of the virus.

6 Numerical Simulation

In order to illustrate the analytical results of the study, numerical simulations of the model in (2.6) is carried out using the set of parameter values in Table (1.2) above. The computation was done using Mathematica software version 9.0. In figure two below, the distribution of human population with time is shown for all the four classes. In figure 1, it was found that the susceptible class decreases with time due to infection with the virus. The class of asymptomatic infected human increases with time as a result of interaction with susceptible human. In figure 1, it was also found that the population of symptomatic and AIDS individuals are increasing with time. The initial state variables are chosen to be $S = 1000, I_1 = 0, I_2 = 0, A = 0$

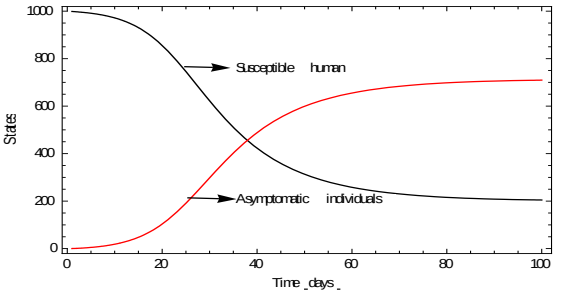

Fig 1: Showing population of susceptible and asymptomatic individuals

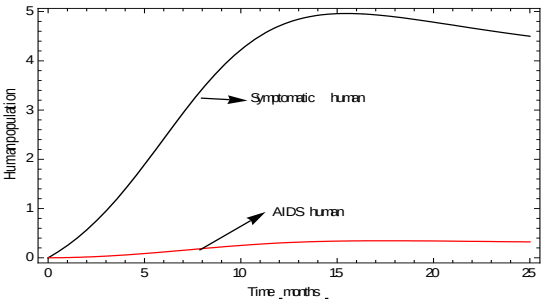

Fig 2: Showing population of symptomatic and AIDS individuals

7 Conclusion

In conclusion, this paper discourses a key public health question on the influence of vertical transmission to the HIV transmission. A nonlinear deterministic mathematical model is considered by incorporating the birth of newborn infected with the virus directly into the infected class. The model also assumed that some infected mothers gave birth to the newborn that are free of virus, as such they added to the population of susceptible class. Some basic properties of the model are investigated and model threshold parameter is also obtained. Sensitivity analysis of the model parameters was carried out, in order to obtain the parameters that help in spreading the virus most. The results of the analysis have shown that, the most sensitive parameter is the contact rate of the susceptible with the asymptomatic infective (β_2). The next sensitive parameter is the number of sexual cohorts of susceptible with the asymptomatic class (c_2). Then, the least sensitive parameter is the fraction of new born susceptible from the infective classes (ε). Thus, it indicates that, the newborn offspring with the virus are much more higher, hence, contributing to the increase of the infective classes. Therefore, the results obtained will help the policy makers and health practitioners on devising the appropriate control strategies on the spread of the disease.

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