

## MATHEMATICAL MODEL FOR CO-INFECTION OF HIV/AIDS AND PNEUMONIA WITH TREATMENT

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**Abstract**— Pneumonia occurs commonly in HIV-infected patients. In this paper, we study a simple mathematical model for the co-infection of HIV/AIDS and Pneumonia. We establish that the model is well presented epidemiologically and mathematically. The disease-free equilibrium point is determined. We establish the basic reproduction number  $R_0$  for the model, which is a measure of the course of co-infection.

**Key words**— *HIV/AIDS –Pneumonia model, Co-infection, basic reproduction number, stability*

### 1. Introduction

The study of infectious disease co-epidemics is critical to understanding how the diseases are related, and how prevention and treatment efforts can be most effective. HIV infection is considered a risk factor for pneumonia both in adults and children [6,14]. The most causative agent is *S. pneumoniae* whose colonisation is increased by HIV infection [6, 14, 32]. Other causative agents include *Staphylococcus aureus* and Gram-negative bacteria and *Pneumocystis jirovecii* (PCP) [5, 6]. In a Kenyan study, the prevalence of oropharyngeal colonization with pneumococci is about 15 percent in HIV infected patients [14]. Incidence of pneumonia is higher in HIV infected individuals than in HIV uninfected individuals [4,23, 24] and it increases with falling CD4 cell count [4, 8, 19]. The risk of invasive disease due to *S. pneumoniae* is estimated to be 40 times more in HIV infected children than HIV negative children [5] and about 25 times higher in HIV infected adults than HIV negative ones [4]. The rate of pneumonia episodes is 0.055 per year for HIV positive and 0.009 for HIV negative [8]. The rates of pneumonia per year ranged from 0.023 to 0.108 for CD4 cell

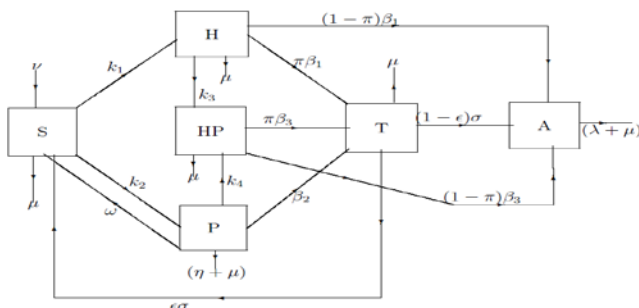
count of  $> 500/mm^3$  to  $< 200/mm^3$  and the rate is 0.02 per year for HIV negative individuals [8, 19]. Mortality due to pneumonia is higher in HIV positive individuals than in uninfected people [5, 24]. There is a three to six fold increase in mortality for HIV infected individuals with pneumonia than those that do not have it [24, 32]. The case fatality rate for acute pneumonia in HIV infected children is 3 to 6 times more than that for HIV negative children [5]. Antiretroviral (ARV) medicines or antiretroviral treatment (ART) are the main type of treatment for HIV/AIDS. ARTs should be initiated when patients have CD4T count below  $200/mm^3$ . It is not a cure but can only prolong the life of a person for many years. ART drugs have to be taken every day for the rest of a person's life. ARTs keep the amount of HIV in the body at low level which retards any weakening of the immune system and allows the body to recover any damage that HIV might have caused. Highly Active Antiretroviral Therapy (HAART) which utilizes two or more drugs can reduce and maintain viral load below the limit of detection in many patients.

### 2. Model Description and Formulation

The total population at any time  $t$ , denoted by  $N(t)$  is subdivided into various mutually exclusive compartments depending on their disease status: Susceptible individuals to both diseases,  $S(t)$ ; individuals infected with HIV at any time,  $t$ ,  $H(t)$ ; those infected with pneumonia,  $P(t)$ ; individuals infected with both HIV and pneumonia,  $HP(t)$ , the total number of individuals on HIV, pneumonia and dual infection treatment at any time,  $t$ ,  $T(t)$  and the number of AIDS patients,  $A(t)$ . This means that

$$N(t) = S(t) + H(t) + P(t) + HP(t) + T(t) + A(t) \quad (1)$$

The rates of infection of susceptible individuals with HIV and Pneumonia are  $k_1$ , and  $k_2$  respectively. Let  $\eta$  and  $\lambda$  be AIDS and Pneumonia induced mortality respectively and suppose  $\mu$  is per capita natural death rate. The constant per capita recruitment rate into the susceptible population is  $\nu$ . The rate at which HIV and pneumonia infected individuals progress for treatment are  $\beta_1$  and  $\beta_2$  respectively. Also let  $\beta_3$  be the rate at which the co-infection progress for treatment. Define  $\sigma$  as the treatment rate,  $\omega$  as the natural recovery rate for pneumonia infectives and  $\epsilon$  as the proportion of pneumonia fully recovered after treatment move to the susceptible class. We assume that the recovered individuals do not acquire immunity to pneumonia or both diseases and thus become susceptible again. We assume that not all HIV infected individuals receive treatment probably due to poor access to health centres, lack of awareness or unwillingness to know the HIV status. So we define  $\pi$  to be the proportion of HIV infected individuals receiving treatment, meaning  $(1-\pi)$  does not receive treatment. From the above definitions and variable, we have the diagram below that illustrate the flow if individuals as they face the possibility of acquiring specific disease infection and co-infection.



**Figure 1:** Flow chart of the transmission dynamics of the co-infection of HIV/AIDS and Pneumonia  
Mathematical equation modeling the above description can be written as follows:

$$\frac{dS}{dt} = \nu + \epsilon \sigma T - (k_1 + k_2 + \mu)S + \omega P$$

$$\frac{dH}{dt} = k_1 S - (k_3 + \beta_1 + \mu)H$$

$$\frac{dHP}{dt} = k_3 H + k_4 P - (\beta_3 + \mu)HP$$

$$\frac{dP}{dt} = k_2 S - (k_4 + \beta_2 + \omega + \eta + \mu)P$$

$$\frac{dT}{dt} = \pi\beta_3 HP + \pi\beta_1 H + \beta_2 P - (\sigma + \mu)T$$

$$\frac{dA}{dt} = (1 - \pi)\beta_1 H + (1 - \epsilon)\sigma T + (1 - \pi)\beta_3 HP - (\lambda + \mu)A \quad (2)$$

### 1. Positivity and Boundedness of solutions

In this section, the basic properties of model system (2) useful for the study and proofs of the stability of the systems are given. The model properties are employed to establish the criteria for positivity of solutions and well-posedness of the system. This model monitors the behaviour of the co-epidemic of the two diseases in human population size that varies and therefore it can be shown that the associated state variables are non-negative for all time  $t \geq 0$  and that the solutions of the model (2) with positive initial data remains positive for all time  $t \geq 0$ . We assume the associated parameters as nonnegative for all time  $t \geq 0$ .

**Theorem 3.1** Every solution of the model equations (2) with initial conditions in  $R_+^6$  approaches and stays in  $\Psi$  as  $t \rightarrow \infty$ .

**Proof:** To show that all feasible solutions are uniformly-bounded in a set  $\Psi$ . We differentiate each term in (1) with respect to time, we have

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dH}{dt} + \frac{dP}{dt} + \frac{dHP}{dt} + \frac{dT}{dt} + \frac{dA}{dt} \quad (3)$$

Adding equations of system (2), we have

$$\begin{aligned} \frac{dN}{dt} = & \nu + \epsilon \sigma T - k_1 S - k_2 S - \mu S + \omega P + k_1 S \\ & - k_3 H - \beta_1 H - \mu H + k_3 H + k_4 P - \beta_3 HP - \mu HP \\ & + k_2 S - k_4 P - \beta_2 P - \omega P - \eta P + \pi\beta_3 HP + \pi\beta_1 H \\ & + \beta_2 P - \sigma T - \mu T + \beta_1 H - \pi\beta_1 H + \sigma T - \epsilon \sigma T \\ & - \beta_3 HP - \pi\beta_3 HP - \lambda A - \mu A \end{aligned} \quad (4)$$

Simplifying equation (4) above gives

$$\frac{dN}{dt} = \nu - (S + H + HP + P + T + A)\mu - \eta P - \lambda A \quad (5)$$

And following equation (1), we see that equation (5) reduces to

$$\frac{dN}{dt} = \nu - \mu N - \eta P - \lambda A \quad (6)$$

In the absence of Pneumonia and AIDS or/and co-infection, equation (6) becomes

$$\frac{dN}{dt} = v - \mu N \quad (7)$$

Applying Birkhoff and Rota's theorem [2] on differential inequality, we have

$$\frac{dN}{dt} \leq v - \mu N \quad (8)$$

Hence by separation of variables,

$$\frac{dN}{v - \mu N} \leq dt \quad (9)$$

Integrating (9) on both sides

$$\int \frac{dN}{v - \mu N} \leq \int dt \quad (10)$$

The integration gives  $-\frac{1}{\mu} \ln(v - \mu N) \leq t + c$  (11)

Where  $c$  is the constant of integration, Inequality (12) simplifies to

$$v - \mu N \geq Ae^{-\mu t} \quad (12)$$

Where  $A$  is a constant. Now, setting  $t = 0$  and applying the initial condition

$$N(0) = N_0 \text{ in (13), we get } A = v - \mu N_0 \quad (13)$$

Which upon substitution in (12) yields,

$$v - \mu N \geq v - \mu N_0 e^{-\mu t} \quad (14)$$

Making  $N$  the subject in (14) we have,

$$N \geq \frac{v}{\mu} - \left[ \frac{v - \mu N_0}{\mu} \right] e^{-\mu t} \quad (15)$$

As  $t \rightarrow \infty$  in (15), the population size,  $N \rightarrow \frac{v}{\mu}$  which implies that  $0 \leq N \leq \frac{v}{\mu}$ . Thus the feasible solutions set of system (2) enter and remain in the region  $\Psi = \left[ (S, H, P, HP, T, A) \in \mathbb{R}^+ : N \leq \frac{v}{\mu} \right]$ . In this case,

whenever  $N \geq \frac{v}{\mu}$  thus, the host population reduces asymptotically to the carrying capacity. On the other hand, whenever  $N \leq \frac{v}{\mu}$ , every solution with initial condition in  $R_+^6$  remains in that region for  $t > 0$ . Thus region  $\Psi$  is positively invariant. Thus every solution of the model equations (2) with initial conditions in  $R_+^6$  approaches and stays in  $\Psi$  as  $t \rightarrow \infty$ . Therefore, the basic model is well posed both epidemiologically and mathematically. Hence it is sufficient to study the dynamics of our model in  $\Psi$ .

The Existence, uniqueness and continuation results also hold for the model (2) in  $\Psi$ . Hence model (2) is well-posed mathematically and epidemiologically and it is sufficient to consider its solutions in  $\Psi$ .

## 2. Disease-free equilibrium point

Disease-free equilibrium (DFE) points of a disease model are its steady-state solutions in the absence of infection or disease. We denote this point by  $E^0$ . Let  $\alpha_1, \alpha_2, \alpha_3$ , and  $\alpha_4$  be per capita contact rates for infections. The model system (2) can be re-written as;

$$\frac{dS}{dt} = v + \varepsilon \sigma T - \frac{\alpha_1(H + \theta HP)}{N} S - \frac{\alpha_2 P}{N} S + \omega P - \mu S$$

$$\frac{dH}{dt} = \frac{\alpha_1(H + \theta HP)}{N} S - \frac{\alpha_3 P}{N} H - (\beta_3 + \mu) H$$

$$\frac{dHP}{dt} = \frac{\alpha_3 P}{N} H + \frac{\alpha_4 P}{N} H - (\beta_3 + \mu) HP \quad (2.1)$$

$$\frac{dP}{dt} = \frac{\alpha_2 P}{N} S - \frac{\alpha_4 H}{N} P - (\beta_2 + \omega + \eta + \mu) P$$

$$\frac{dT}{dt} = \pi \beta_3 HP + \pi \beta_1 H + \beta_2 P - (\sigma + \mu) T$$

$$\frac{dA}{dt} = (1 - \pi) \beta_1 H + (1 - \mu) \sigma T + (1 - \pi) \beta_3 HP - (\lambda + \mu) A$$

The Disease Free Equilibrium (DFE) of the model system (2.1) is obtained by setting;

$$\frac{dH}{dt} = \frac{dP}{dt} = \frac{dHP}{dt} = \frac{dT}{dt} = \frac{dA}{dt} = 0$$

At disease free equilibrium, it is assumed that there are no infections. Then we set

$$\frac{H}{N} = \frac{P}{N} = \frac{HP}{N} = \frac{T}{N} = \frac{A}{N} = 0$$

and substitute this in the system of equations (2.1), the system reduces to;

$$v - v \frac{S}{N} = 0$$

Therefore

$$v = v \frac{S}{N}$$

Implying that

$$\frac{S}{N} = 1$$

But at disease free equilibrium, the susceptible population is equal to total population, that is to say

$$\frac{S}{N} = 1$$

So the Disease Free Equilibrium,  $E^0$  of the full model (2.1) is given by

$$E^0 = \left( \frac{S}{N}, 0, 0, 0, 0, 0 \right) = (1, 0, 0, 0, 0, 0)$$

### 3. The Basic Reproduction Number, $R_0$

The basic reproduction number is defined as the expected number of secondary infections produced by an index case in a completely susceptible population [3]. We define the basic reproduction number,  $R_0$  as the number of secondary HIV (or Pneumonia) infections due to a single HIV (or a single pneumonia -infective) individual. We determine  $R_0$  using the next generation operator approach [27]. The associated next generation matrices are

$$F = \begin{pmatrix} \alpha_1 & 0 & \theta\alpha_1 & 0 & 0 \\ 0 & \alpha_2 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

$$V = \begin{pmatrix} \beta_1 + \mu & 0 & 0 & 0 & 0 \\ 0 & \beta_2 + \omega + \eta + \mu & 0 & 0 & 0 \\ 0 & 0 & \beta_3 + \mu & 0 & 0 \\ -\pi\beta_1 & \beta_2 & -\pi\beta_3 & \sigma + \mu & 0 \\ (1 - \pi)\beta_1 & 0 & -(1 - \pi)\beta_3 & -\sigma(1 - \epsilon) & \lambda + \mu \end{pmatrix}$$

The basic reproduction number  $R_0$  is the spectral radius of the matrix  $FV^{-1}$ .

$$FV^{-1} = \begin{pmatrix} \frac{\alpha_1}{\beta_1 + \mu} & 0 & \frac{\theta\alpha_1\beta_2\beta_3(1-\pi)}{(\beta_2 + \omega + \eta + \mu)(\sigma + \mu)(\lambda + \mu)} & 0 & 0 \\ 0 & \frac{\alpha_2}{\beta_2 + \omega + \eta + \mu} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

The eigenvalues of the matrix  $FV^{-1}$  are  $\frac{\alpha_1}{\beta_1 + \mu}$ ,  $\frac{\alpha_2}{\beta_2 + \omega + \eta + \mu}$ , 0, 0, 0

It follows that the basic reproduction number which is given by the largest Eigenvalue for the model of HIV and AIDS and Pneumonia co-infection with treatment denoted by  $R_0$  is given by

$$R_0 = \max \left\{ \frac{\alpha_1}{\beta_1 + \mu}, \frac{\alpha_2}{\beta_2 + \omega + \eta + \mu} \right\}$$

Denoting  $R_{(HIV)} = \frac{\alpha_1}{\beta_1 + \mu}$  and  $R_{(pneu)} = \frac{\alpha_2}{\beta_2 + \omega + \eta + \mu}$

$R_{(HIV)}$  is a measure of the average number of secondary HIV infections caused by a single infective introduced into an entirely susceptible population. Similarly,  $R_{(pneu)}$  is a measure of the average number of secondary pneumonia infections in humans caused by a single infective human introduced into an entirely susceptible population. The following lemma follows from Theorem 2 of [27].

**Lemma 5.1:** The the disease-free equilibrium  $E^0$  of the model (2.1) is locally asymptotically stable whenever  $R_0 < 1$  and unstable when  $R_0 > 1$ .

### Conclusion

The importance of an epidemiological model lies in its ability to provide meaningful biological interpretations and the possible disease control measures. The implication of this is that  $R_{(pneu)} \rightarrow 0$  and thus no new

pneumonia infections, and rate of progression to AIDS class reduces. We recommend the treatment of pneumonia be promptly done to help boost the immune system which in turn reduces the progression rate to AIDS class.

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