Analysis of a non-integer order model for the coinfection of HIV and HSV-2

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Abstract: We propose a non-integer order model for the dynamics of the coinfection of HIV and HSV-2. We calculate the reproduction number of the model and study the local stability of the disease-free equilibrium. Simulations of the model for the variation of epidemiologically relevant parameters and the order of the non-integer order derivative, α, reveal interesting dynamics. These results are discussed from an epidemiologically point of view.

Keywords: non-integer order mathematical model, HIV, HSV-2, coinfection

1. INTRODUCTION

HSV-2 and HIV fuel each other. HSV-2 infection increases the risk of acquiring a new HIV infection by approximately three times. In addition, people coinfected with HIV and HSV-2 are more likely to spread HIV to others. HSV-2 is one of the most common infections in people infected with HIV, occurring in 60-90% of the cases. HSV-2 in co-infected persons presents greater severity and more frequent recurrences. Moreover, in the more advanced stage of HIV, HSV-2 can lead to more serious but rare complications such as meningoencephalitis, esophagitis, hepatitis, pneumonitis, retinal necrosis, or disseminated infection, cf. WHO (2017). Several mathematical models have been derived with the purpose of understanding the dynamics of HIV and HSV-2 coinfection. In 2015, cf. Basak et al. (2015) develop a model for the co-infection of HIV and HSV-2. Numerical simulations suggest that the HSV-2 infected individuals are at higher risk of acquiring HIV infection when compared to HSV-2 non infected individuals. It suggests that reducing the effective contact rate of HSV-2 may reduce the disease burden of the co-infection. On the other hand, controlling the transfer rate from HIV class to AIDS class and the control of the transfer rate of the HSV-2 exposed class to the class infected with HSV-2 are also feasible.

Some Concepts of Fractional Calculus

Fractional calculus (FC) is a generalization to an arbitrary (non-integer) order of ordinary differentiation and integration. Leibniz and Lagrange were the first mathematicians to discover and unravel the power of FC. Fractional models have been used in the literature to understand the behaviour of epidemiological models, where the integer-order models fail to give a complete explanation, cf. Arafa et al. (2013); Pinto and Carvalho (2017).

Driven by the aforementioned research, we analyse the dynamics of the HIV and HSV-2 coinfection in a non-integer order mathematical model. In Section 2, we introduce the model. Numerical simulations of the model for distinct values of the order of the fractional derivative and relevant parameters, are presented and discussed in Section 3. Finally, in Section 4, we conclude our work.

2. THE MODEL

In this section, we describe the proposed non-integer order model. The population of the model is divided in ten classes. Susceptible individuals, S, are recruited at rate Π^α. They are infected with HSV-2 at rate $\lambda_1 = \frac{\beta_1^\alpha (I+\theta(Q+Q_H)+\eta I_H)}{N}$, where β_1^α is the transmission rate of HSV-2, and θ and η are modification parameters. Parameter θ, $(0 < \theta < 1)$ models the fact that infectious individuals in the quiescent stage are less infectious. On the contrary, parameter $\eta > 1$ accounts for the increased infectiousness of the coinfected individuals (I_H). Similarly, individuals S are infected with HIV at rate $\lambda_2 = \frac{\beta_2^\alpha (H+E_H+\eta I_H+\theta Q_H)}{N}$, where β_2^α is the HIV transmission rate. All individuals die by natural causes at rate μ^α. Individuals in the latent stage of HSV-2, E, are infected with HIV at rate λ_2 and progress in HSV-2 infection, for the acute phase, at rate σ_1^α. Individuals in the acute phase of HSV-2, I, are infected with HIV at rate λ_2 and move to the quiescent state, at rate q^α. Individuals in the quiescent stage of the HSV-2, Q, return to the acute phase of infection, at rate r^α and are infected with HIV at rate λ_2. Individuals infected with HSV-2, in the acute or quiescent stage, die at rate τ_1^α. Individuals infected with HIV, H, are infected with HSV-2 at rate λ_1 and develop AIDS at rate ρ_1^α. The AIDS induced mortality rate is τ_2^α. Individuals in the latent stage of HSV-2 and infected with HIV, E_H, progress to the acute phase of HSV infection, at rate σ_2^α, and develop AIDS at rate σ_3^α.

Individuals coinfected with HSV-2 and HIV, I_H, move to the quiescent state of the HSV-2 infection, at rate q_H^α and progress in HIV infection at rate σ_4^α. The individuals in the quiescent stage of HSV-2 and infected with HIV, Q_H, return to the acute phase of HSV-2 infection, at rate r_H^α and develop AIDS, at rate σ_5^α. The non-linear system of fractional order ordinary differential equations describing the dynamics of the model is:

$$\begin{aligned}
\frac{d^\alpha S}{dt^\alpha} &= \Pi^\alpha - \lambda_1 S - \lambda_2 S - \mu^\alpha S \\
\frac{d^\alpha E}{dt^\alpha} &= \lambda_1 S - (\lambda_2 + \sigma_1^\alpha + \mu^\alpha) E \\
\frac{d^\alpha I}{dt^\alpha} &= \sigma_1^\alpha E + r^\alpha Q - (\lambda_2 + q^\alpha + \mu^\alpha + \tau_1^\alpha) I \\
\frac{d^\alpha Q}{dt^\alpha} &= q^\alpha I - (\lambda_2 + r^\alpha + \mu^\alpha + \tau_1^\alpha) Q \\
\frac{d^\alpha H}{dt^\alpha} &= \lambda_2 S - (\lambda_1 + \rho_1^\alpha + \mu^\alpha) H \\
\frac{d^\alpha A}{dt^\alpha} &= \rho_1^\alpha H - (\mu^\alpha + \tau_2^\alpha) A \\
\frac{d^\alpha E_H}{dt^\alpha} &= \lambda_1 H + \lambda_2 E - (\sigma_2^\alpha + \sigma_3^\alpha + \mu^\alpha) E_H \\
\frac{d^\alpha I_H}{dt^\alpha} &= \sigma_2^\alpha E_H + \lambda_2 I + r_H^\alpha Q_H - (\sigma_4^\alpha + q_H^\alpha + \mu^\alpha + \tau_1^\alpha) I_H \\
\frac{d^\alpha Q_H}{dt^\alpha} &= q_H^\alpha I_H + \lambda_2 Q - (r_H^\alpha + \sigma_5^\alpha + \mu^\alpha + \tau_1^\alpha) Q_H \\
\frac{d^\alpha A_H}{dt^\alpha} &= \sigma_3^\alpha E_H + \sigma_4^\alpha I_H + \sigma_5^\alpha Q_H - (\mu^\alpha + \tau_2^\alpha) A_H
\end{aligned} \tag{1}$$

The reproduction numbers of the HSV-2 and HIV sub-models are given by:

$$R_1 = \rho(F_1 V_1^{-1}) = \frac{\beta_1^\alpha \sigma_1^\alpha (\theta q^\alpha + \mu^\alpha + r^\alpha + \tau_1^\alpha)}{(\sigma_1^\alpha + \mu^\alpha)(\mu^\alpha + \tau_1^\alpha)(q^\alpha + r^\alpha + \mu^\alpha + \tau_1^\alpha)} \text{ and}$$

$$R_2 = \rho(F_2 V_2^{-1}) = \frac{\beta_2^\alpha}{\rho_1^\alpha + \mu^\alpha} \tag{2}$$

respectively. Thus, R_0, the reproduction number of the full model is:

$$R_0 = \rho(FV^{-1}) = \max\{R_1, R_2\} \tag{3}$$

Lemma 1. The disease-free equilibrium of the system (1) is unstable if $R_0 > 1$.

3. NUMERICAL SIMULATIONS

We simulate the model (1) for different values of the order of the fractional derivative, α, and for relevant parameters. Parameters used in the simulations are: $\beta_1 = 0.06$, $\theta = 0.4$, $\eta = 1.1$, $\beta_2 = 0.055$, $\Pi = \frac{60000}{1000\times 365}$, $\mu = 0.0027$, $\sigma_1 = 0.04$, $r = 0.4$, $q = 0.2$, $\tau_1 = 0.04$, $\rho_1 = 0.4$, $\tau_2 = 0.09$, $\sigma_2 = 0.4$, $\sigma_3 = 0.6$, $r_H = 0.03$, $q_H = 0.03$, $\sigma_4 = 0.4$, $\sigma_5 = 0.3$, and the inicial conditions are: $S(0) = 5000$, $E(0) = 1000$, $I(0) = 500$, $Q(0) = 100$, $H(0) = 1000$, $A(0) = 200$, $E_H(0) = 1000$, $I_H(0) = 500$, $Q_H(0) = 250$ and $A_H(0) = 100$ Basak et al. (2015). We study how the basic reproduction number R_0 varies with r, the backward transmission between the HSV-2 infected individuals, I, and the individuals in the quiescent stage of HSV-2, Q, and with q, the forward transmission between the HSV-2 infected individuals, I, and the individuals in the quiescent stage of HSV-2, Q. Figures 1-2 show that increasing values of r and decreasing values of q boost higher values of R_0. This suggests that controlling transfer rates between I individuals and Q individuals reduces the burden of the disease. This behaviour is repeated for all values of α.

4. CONCLUSION

We propose a non-integer order model for HIV and HSV-2 co-infection. Numerical results of the model suggest that the backward and forward transmission rates between the HSV-2 infected individuals, I, and the individuals in the quiescent stage of HSV-2, Q, can explain the effect of HSV-2 infection on the values of HIV prevalence. Thus, reducing these rates would possibly control the infection. The order of the fractional derivative, α, may be used to distinguish patients when doing fitting data from real patients. Specificities of patients, namely, age, immune system profile, etc, can be well addressed by α, without changing the structure of the model.

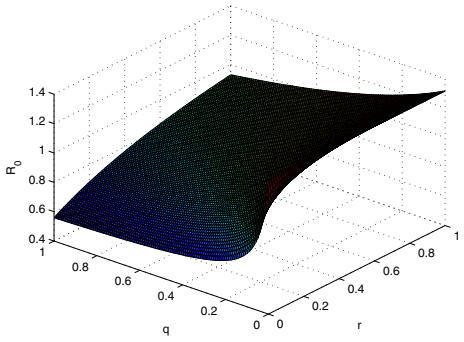

Fig. 1. Effect of r and q, on R_0, for $\alpha = 1$. Parameter values and initial conditions in the text.

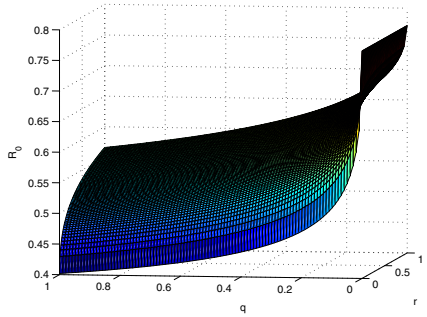

Fig. 2. Effect of r and q, on R_0, for $\alpha = 0.5$. Parameter values and initial conditions in the text.

ACKNOWLEDGEMENTS

Authors were partially funded by the European Regional Development Fund through the program COMPETE and by the Portuguese Government through the FCT under the project PEst-C/MAT/UI0144/2013. AC was partially supported by a FCT grant with reference SFRH/BD/96816/2013.

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