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Stability of Passive Immunisation and Efficacy of Vaccines of Hepatitis B Model

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Abstract: The phenomenon of passive immunisation in disease control models, where a stable epidemic equilibrium state co exist with a stable disease free equilibrium when associated eigen values are all negative, has important implication for disease control. In this study, we modelled the effect of passive immunisation and infectious hepatitis B treatment on the spread and control of the disease. We established the existence of equilibrium states and analyse the disease free equilibrium for stability. It was established that $\lambda_1 = -\mu$, $\lambda_2 = -\mu$, $\lambda_3 = -(\gamma + \mu)$ and $\lambda_4 = (\delta B / \mu) - \mu$ hence, the disease free equilibrium state will be stable if $(\delta B / \mu) < \mu$ i.e., (number of susceptible individuals produced is less than natural death rate). Thus, effort should be intensify in increasing the duration of efficacy of the vaccines used in passive immunisation programme.

Key words: Equilibrium state, epidemic, Hepatitis B, immunisation, passive, stability, vaccines

INTRODUCTION

Compartmental mathematical models have been widely used to gain more insights into the spread and control of emerging and re-emerging human disease dating back to the pioneering work of Bernoulli in 1760 and the likes of Ross, Kermack and Mc Kendrick and others Anderson and May (1992). Hepatitis was first identified as being transmitted through blood in Germany in 1883, but it was not until 1947 that the term Hepatitis B virus (HBV) was proposed.

Hepatitis means inflammation of the liver cells Macpherson (1992-2002), which may be acute or chronic. Hepatitis B virus, the most serious type of viral hepatitis (WHO, 2000-2008) can cause acute infection, chronic carrier status and chronic hepatitis. Hepatitis B virus is the only hepatitis virus causing chronic hepatitis that is vaccine preventable. Hepatitis B virus is transmitted through blood or body fluids in the same way as Human Immunodeficiency Virus (HIV) although hepatitis B virus is 50-100 times more infectious than human immunodeficiency virus (WHO, 2001, 2002). Hepatitis B virus is the most common most common cause of serious infection in the world. It is estimated that worldwide more than two billion people have been infected by hepatitis B virus and 350 million people have chronic infectious hepatitis Drosten *et al*. (2004). Nigeria is classified among the group of countries highly endemic for hepatitis B virus infection. About 75% of the Nigerian population is reportedly likely to have been exposed to hepatitis B virus at one time or the other in their life Sirisena *et al*. (2002). Co-infection with HBV and HIV is a rapidly growing public health concern. The Sub-Saharan Africa has been most severely affected by the HIV/AIDS pandemic with almost 9% of its adult population leaving with HIV (WHO, 2003-2007). Mathematical models have played a key role in the formulation of hepatitis B control strategies and the establishment of internal goal for intervention programs. Most of these models are the SEIR class in which the host population is categorised by infection status as susceptible, exposed (infectious but not yet infectious), infectious and recovered. One of the principle attributes of these models is that the force of infection (the rate at which susceptible leave the susceptible class and move into the infected category) is a function of the number of infectious hosts in the population at any time t and is thus, a non linear term. Other transitions such as the recovery of infectious individuals and death are modelled as linear terms with constant coefficients. This study therefore attempts to use mathematical modelling to explain how the spread of hepatitis B can be controlled across Nigeria.

METHODOLOGY

Model description: The M-S-I-R model is partitioned into compartments of passively immune infants (M), susceptible individuals (S), infectious individuals (I) and removed individuals (R).The immunised compartment changes due to the coming in of the immunised children into the population where we assumed that a proportion of B of the incoming individuals are immunised against infection. This compartment reduces due to expiration of duration of vaccines efficacy at the rate δ and also by natural death at the rate μ. The susceptible population increases due to the coming of individual from the the expiration of duration of vaccines efficacy at the rate δ. The susceptible population also reduces due to natural

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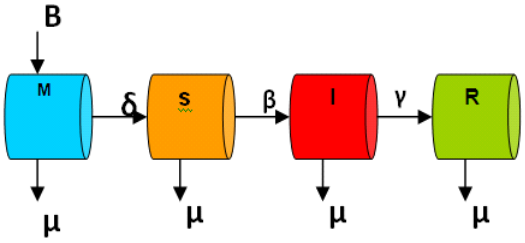

Fig. 1: Schematic representation of the model

death at the rate μ and infection within a contact rate of infection β. In the same way the population dynamic of the infectious class grows with the incidence rate of infection βSI. This class also reduces by natural death rate μ and successful cure of infectious hepatitis B patients at the rate γ.

Lastly the dynamics of the removed with immunity class increases with successful cure of infectious hepatitis B patients at the rate γ and decrease by natural death rate μ. A schematic description of the model one is given in Fig. 1. Keeping in view of these assumptions, our population dynamic, i.e., "passively immune infant-susceptible- infectious-removed" is governed by the following set of differential equations:

$$dM / dT = B - \delta MS - \mu M \quad (1)$$

$$dS / dT = \delta MS - \beta SI - \mu S \quad (2)$$

$$dI / dT = \beta SI - \gamma I - \mu I \quad (3)$$

$$dR / dT = \gamma I - \mu R \quad (4)$$

where; total population at any instantt is N(t) = M(t) + S(t) + I(t) + R(t). Now, in the above system (1)-(4), use the following and:

$$dM / dt = dS / dt = dI / dt = dR / dt = 0$$

and

$$M(t) = w, S(t) = x, T(t) = y, R(t) = z$$

to get the following re-scaled system:

$$B - \delta wx - \mu w = 0 \quad (5)$$

$$\delta wx - \beta xy - \mu x = 0 \quad (6)$$

$$\beta xy - \gamma y - \mu y = 0 \quad (7)$$

$$\gamma y - \mu z = 0 \quad (8)$$

In the next section, we will study the existence of disease free equilibrium state and the epidemic equilibrium state. Existence of equilibrium states of the model:

Disease free equilibrium state: From (7):

$$\beta xy - \gamma y - \mu y = 0$$
$$(\beta x - \gamma - \mu)y = 0$$
$$y = 0 \quad (9)$$

or

$$\beta x - \gamma - \mu = 0 \quad (10)$$

Substituting (9) for y in (6) we obtained:

$$\delta wx - x\gamma - \mu x = 0$$
$$\delta wx - \mu\gamma = 0$$
$$(\delta w - \mu)x = 0$$
$$x = 0 \quad (11)$$

or

$$\delta w - \mu = 0 \quad (12)$$

Substituting (11) into (5) we obtained:

$$B - \delta wx - \mu w = 0$$
$$B - \mu w = 0$$
$$\mu w = B$$
$$w = B/\mu \quad (13)$$

Substituting (9) into (8) we obtained:

$$\gamma y - \mu z = 0$$
$$\mu z = 0$$
$$\gamma Y - \mu z = 0$$
$$\mu z = 0$$
$$z = 0 \quad (14)$$

Hence the disease free equilibrium state is:

$$E_1 = (B/\mu, 0, 0, 0) \quad (15)$$

The Epidemic equilibrium state: From (10) we have:

$$\beta x - \gamma - \mu = 0$$
$$\beta x = (\gamma + \mu)$$
$$x^* = (\gamma + \mu) / \beta \quad (16)$$

Substituting (16) for x in (5) we obtained:

$$B - \delta wx - \mu w = 0$$

$$B - \frac{\delta w(\gamma + \mu)}{\beta} + \mu w = 0$$

$$B - \left[\delta \frac{(\gamma + \mu)}{\beta} + \mu\right] w = 0$$

$$B - \left[\frac{\delta(\gamma + \mu) + \beta\mu}{\beta}\right] w = 0$$

$$\left[\frac{\delta(\gamma+\mu)+\beta\mu}{\beta}\right]w = B$$

$$w^* = \frac{B\beta}{\left[\delta(\gamma+\mu)+\beta\mu\right]} \quad (17)$$

Substituting (16) for x and (17) for w in (6) we obtained:

$$\delta wx - \beta xy - \mu x = 0$$

$$\frac{\delta B\beta(\gamma+\mu)}{\left[\delta(\gamma+\mu)+\beta\mu\right]\beta} - \frac{\beta(\gamma+\mu)y}{\beta} - \frac{\mu(\gamma+\mu)}{\beta} = 0$$

$$\left(\delta\beta B(\gamma+\mu) - \beta\left[\delta(\gamma+\mu)+\beta\mu\right](\gamma+\mu)y - \mu(\gamma+\mu)\left[\delta(\gamma+\mu)+\mu\beta\right]\right) / \left[\delta(\gamma+\mu)+\beta\mu\right]\beta$$

$$\beta\left[\delta(\gamma+\mu)+\beta\mu\right](\gamma+\mu)y = \delta\beta B(\gamma+\mu) - \mu(\gamma+\mu)\left[\delta(\gamma+\mu)+\beta\mu\right] = 0$$

$$y = \frac{\delta\beta B(\gamma+\mu) - \mu(\gamma+\mu)\left[\delta(\gamma+\mu)+\beta\mu\right]}{\beta\left[\delta(\gamma+\mu)+\beta\mu\right](\gamma+\mu)}$$

$$y^* = \frac{\delta\beta B - \mu\left[\delta(\gamma+\mu)+\beta\mu\right]}{\beta\left[\delta(\gamma+\mu)+\beta\mu\right]} \quad (18)$$

Substituting (18) for y in (8) we obtained:

$$\gamma y - \mu z = 0, \quad \mu z = \gamma y$$

$$\Rightarrow z = \left[\frac{\delta\beta B - \mu\left[\delta(\gamma+\mu)+\mu\beta\right]}{\beta\left[\delta(\gamma+\mu)+\mu\beta\right]\mu}\right]$$

$$z^* = \frac{\gamma\delta\beta B - \mu\left[\delta(\gamma+\mu)+\mu\beta\right]\gamma}{\beta\left[\delta(\gamma+\mu)+\beta\mu\right]\mu} \quad (19)$$

Hence the epidemic equilibrium state is given by:

$$E^* = (w^*, x^*, y^*, z^*)$$

Dynamical behaviour of the system: Stability analysis of the disease free equilibrium state: We have already established that the system (5)-(8) has disease free equilibrium state, $E_1 = (B/\mu, 0, 0, 0)$ and epidemic equilibrium state $E^* = (w^*, x^*, y^*, z^*)$ in the previous section. Again, the general variational matrix corresponding to the system is given by:

$$J = \begin{pmatrix} -(\delta x+\mu) & -\delta w & 0 & 0 \\ \delta x & \delta w - \beta y - \mu & -\beta x & 0 \\ 0 & \beta y & \beta x - \gamma - \mu & 0 \\ 0 & 0 & 0 & -\mu \end{pmatrix} \quad (20)$$

The characteristic equation is obtained from the Jacobian determinant with the eigen values λ:

$$-(\delta x+\mu) - \lambda\left[(\delta w - \beta y - \mu - \lambda)(\beta x - y - \mu - \lambda)(-\mu-\lambda) + \beta x\beta y(-\mu-\lambda)\right] + \delta w\left[\delta x(\beta x - y - \mu - \lambda)(-\mu-\lambda)\right] = 0 \quad (21)$$

At disease free equilibrium state substituting (15) into (21) we obtained:

$$\left(-\mu-\lambda^2\right)\left(\frac{\delta B}{\mu} - \mu - \lambda\right)\left(-\gamma-\mu-\lambda\right) = 0$$

$$\Rightarrow$$

$$\lambda_1 = -\mu$$

$$\lambda_2 = -\mu$$

$$\lambda_3 = -(\gamma+\mu)$$

$$\lambda_4 = \left(\frac{\delta B}{\mu} - \mu\right)$$

Note that λ_1, λ_2 and λ_3 are all negative, the disease free equilibrium state will be stable if $\delta B/\mu < \mu$. Where $\delta B/\mu$ is the number of susceptible individuals produced.

Theorem 1: The system (5)-(8) is locally stable around the disease free equilibrium state E_1, when $\delta B/\mu < \mu$. This implies that the susceptible individuals produce must be less than the natural death rate.

CONCLUSION

Hepatitis B is a contagious disease and therefore preventive and control of the disease could be achieved if the following measures are adopted. Individuals should practice safe sex, not share personal care items that might have blood on them (razors, toothbrushes). Government and other immunization partners should strengthen routine HBV immunization programme and effort should be intensify in increasing the duration of efficacy of the vaccines used in passive immunisation programme.

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