Australian Journal of Basic and Applied Sciences

2022 September; 16(9): pages 1-11
DOI: 10.22587/ajbas.2022.16.9.1

Original paper AENSI Publications

Analysis of an SEIR model with the vertical transmission on transmission and spread of hepatitis B in Ghana

***Kwaafo Akoto Awuah-Mensah[a], Ute Mueller[b], Steven Richardson[c]**

[a]School of Natural and Environmental Sciences (SNES), University of Environment and Sustainable Development (UESD), Somanya-Ghana
[a;b;c] School of Science, Edith Cowan University, Joondalup, WA 6027, Australia

Correspondence Author: Kwaafo Akoto Awuah-Mensah, School of Natural and Environmental Sciences (SNES), University of Environment and Sustainable Development (UESD), Somanya-Ghana.
School of Science, Edith Cowan University, Joondalup, WA 6027, Australia Email: rezendeleonardo77@yahoo.com

Received date: 12 January 2021, Accepted date: 24 April, Online date: 15 September 2022

Citation: K.A. Awuah-Mensah, Ute Mueller, S. Richardson, 2022. Analysis of an SEIR model with the vertical transmission on transmission and spread of hepatitis B in Ghana. Australian Journal of Basic and Applied Sciences, 16(9): 1-11. DOI: 10.22587/ajbas.2022.16.9.1.

ABSTRACT: Lack of good quality information about hepatitis B (HB) is a major hindrance to policy direction and comprehensive implementation of interventions to prevent and control the disease in the endemic region of Sub-Saharan Africa (SSA), particularly Ghana. A SEIR deterministic compartmental model which incorporates latent period and vertical transmission, and applied to HB incidence data was used to examine the transmission and spread of HB in order to inform policy decision on prevention and control of the disease in a population. The model parameters were estimated by a unique hybrid optimisation method involving Genetic Algorithm and Levenberg Marquardt Algorithm using MATLAB (version R2018a). Based on the estimated parameters, the epidemiological threshold parameter R_0 was calculated to determine the prediction of the disease. The model was found to have a disease-free equilibrium that is globally asymptotically stable when the epidemiological threshold parameter $R_0 \leq 1$, and an unique endemic equilibrium that is asymptotically stable when $R_0 > 1$. Stability of the model was discussed in terms of proportions of the state variables, where disease eradication or persistence meant the total infected proportions $e + i$ vanished or uniformly persisted respectively with time. The threshold parameter, based on the estimated parameters, was calculated to be $R_0 = 1.6854$, which indicated that HB persists in the population. The endemic equilibrium state $Q^* = (0.5741, 0.0706, 0.3553)$ was stable with total infected proportion 0.4.3 of the population uniformly persisting with time. Vertical transmission was found to be the major drive to transmission and spread of HB, compared with other parameters, and achieving a herd immunity threshold $H = 0.4067$ of the population would keep the disease under control. The study also revealed that latent period is important in modelling HB.

Keywords: Epidemiological threshold parameter, Hepatitis B, SEIR model, Infectious disease, Vertical transmission

INTRODUCTION

HB is a global health concern responsible for more than 780,000 deaths per year; over 240 million people are estimated to have a chronic infection (WHO, 2020, 2016). The disease has caused epidemics in Asia and Africa and is endemic in China. World Health Organisation (WHO) global reports indicated that one out of every three of the world's population had been infected with the disease (WHO, 2020, 2016). Africa, about 12% of the world's population, carries 18% of the global burden of HB and 6.1% of the adult population is infected (WHO, 2020; Kramvis and Kew, 2007). Rated second to tobacco globally as a major cause of human malignancy, the disease is also known to be a major cause of death of HIV/AIDS co-infected individuals (Locarnini et al., 2013). Poor management of hepatitis B/ hepatitis C virus (HBV/HCV) co-infection has resulted in high-risk levels of mortality of HIV-positive patients in SSA (Aoudjane et al., 2014; Hawkins et al., 2013). However, most countries lack precise disease burden data even though available information indicates that the load is considerable (WHO, 2020; Wiktor, 2015).

WHO's health assembly resolution (2010) on HB requested member states to generate a reliable database relevant to building interventions suitable for the regional epidemiological profile and health systems capacities (WHO, 2016). Despite this call, many developing countries where HB is endemic have poor-quality data on the burden of the disease due to inefficient data collection tools and economic challenges (Kramvis and Kew, 2007; Wiktor, 2015; Compston et al., 2009).

HB is a viral disease characterised by a broad spectrum of clinical outcomes ranging from asymptomatic hepatitis to fulminant liver failure (WHO, 2020). One becomes infected with Hepatitis B Virus (HBV) by exposure to contaminated blood and body fluids. The main transmission routes are horizontal (person-to-person) and vertical (mother-to-child). Some studies have suggested that vertical transmission is uncommon in Africa, but others indicated that vertical transmission is greater in SSA and Asia than in other developing countries (Ott et al., 2012; WHO, 2020). Vertical transmission most likely occurs at birth, but in rare cases can be intrauterine or postpartum (Ott et al., 2012; Gentile I, 2014). The virus can incubate for a period of 75 days on average, ranging from 30 to 180 days or more depending on the infected person's viral load (WHO, 2020). Failure to clear the disease at the acute stage leads to chronic carriage, which may progress to liver cirrhosis and hepatocelular carcinoma without antiviral treatment (WHO, 2020).

Mathematical modelling has served as a tool to provide a theoretical framework for understanding the epidemiology of infectious diseases in a population (Nelson et al., 2001). Compartmental modelling has also been used extensively to provide deep understanding about the spread and control of infectious diseases (Xin-zhu et al., 2007). However, compartmental modelling of HB has not been well studied in SSA, particularly Ghana (Dontwi et al., 2014; Wearing et al., 2005). After reviewing the literature, this is the first attempt to apply compartmental modelling coupled with a unique hybrid optimisation technique to HB incidence data to comprehensively examine the transmission and spread of the disease in a geographically isolated and endemic setting of Ghana in SSA. This study sought to apply an appropriate SEIR deterministic compartmental model and a unique hybrid optimisation method to HB incidence data to examine and predict the transmission and spread of the disease in a population of varying sizes. These methods will apply to HB incidence data from similar settings whilst the outcome will be useful to inform policy decisions towards managing the pandemic in Ghana, and by extension any similar endemic setting in the SSA.

2. MATERIALS AND METHODS

2.1 Data Description

The main data for the study consisted of reported but de-identified, monthly incidence cases of HB. The data were categorised into cases of persons aged < 5 years; that were assumed to be vertically transmitted and those aged ≥ 5 from all other transmission routes (Gentile I, 2014). The data were aggregated for the ten regions of Ghana covering the period from 2008 to 2014. The data were obtained from the Regional Health Informant Units (RIU) and Center for Health Information Management (CHIM) of the Ghana Health Service (GHS) (Ministry of Health Ghana, 2014). The descriptive statistics of the data were summarised and displayed in Table 1. In addition to the incidence data, demographic parameter constants of the total population $N = 27{,}075.827$, and natural birth and death rates $\lambda = 24.9$ and $\mu = 6.6$ per 1.000 population, r were sourced from Ghana Statistical Service (GSS) (GSS, 2014). The time series and cumulative incidence plots of the incidence data for the stated period are displayed in Figures 1 and 2, respectively. While the time series incidence plot shows a fluctuating but increasing trend, the cumulative incidence plot shows a steady increase over the period.

Table 1: Summary of HB incidence data collected.

Region	Min.	Max.	Mean	Median	Standard deviation	Total incidence
Ghana	372	2,789	1,368.18	1,371	630.54	114,927
Vertical Transmission (Incidence aged 55)	28	323	103.93	83	68.51	8,730
All other routes (Incidence aged ≥ 5)	341	2,611	1,264.25	1,288.5	579.6	106,197

2.2 Model description

In this study, the SEIR model employed divides the population into four mutually exclusive compartments namely Susceptible (S), Exposed (E), Infectious (I) and Recovered (R). The disease progression of an infected individual through the compartments of the model is illustrated by Figure 3. The parameter constants N, λ and μ are total population, natural birth rate, and natural death rate respectively. Furthermore, β is the effective infectious contact rate, γ is the rate of removal from the exposed class and ν is the recovery rate. The SEIR model also incorporates the proportionate incidence rate $\frac{\beta SI}{N}$, vertical transmission, and latent

period which is all found to be critical in modelling HB (WHO, 2016; CDCP, 2016). Vertical transmission rate α which represents the number of newborns per 1.000 population who present with HB was estimated by

$$\alpha = \frac{\text{incidence aged } <5}{\text{total incidence}} \times \lambda = 0.076\lambda \qquad (2.1)$$

where incidence aged < 5 represents the number of incidence cases via vertical transmission and total incidence (incidence aged $< 5 +$ incidence aged ≥ 5) corresponds to total infection $I + E$ in the model. The system of nonlinear differential equations defines the model

$$\begin{aligned} \frac{dS}{dt} &= \lambda N - \alpha(I+E) - \beta\frac{SI}{N} - \mu.S \\ \frac{dE}{dt} &= \beta\frac{SI}{N} + \alpha(I+E) - \mu E - \gamma E \\ \frac{dI}{dt} &= \gamma E - \mu I - \nu I \\ \frac{dR}{dt} &= \nu I - \mu R \end{aligned} \qquad (2.2)$$

where $S(t), E(t).I(t)$ and $R(t)$ are nonnegative and $N(t) = S(t) + E(t) + I(t) + R(t)$. The mean latent and infectious periods are defined by $1/(\lambda + \gamma)$ and $1/(\lambda + \nu)$, respectively (Smith et al., 2001)

The assumptions of the model were:

- The population is homogeneously mixed with respect to the compartments and that guarantees mass-action in host interaction. Thus the population density of identifiable local geographical area within the population was considered to be fixed although the global population size $N(t)$ may vary with time so that $\frac{dN}{dt} = (\lambda - \mu)N$.
- Horizontal transmission of disease was described as the effective close physical contact between an infectious person and a susceptible person, and represented by the rate $\beta\frac{SI}{N}$.
- Vertical transmission was represented by a fraction. a, of the total infected population, and $\alpha(I + F_i)$ and $\lambda N - \alpha(I + F_i)$ are birth fluxes recruited via the exposed and susceptible compartments respectively.
- The recovered hosts have permanent immunity and cannot re-enter the susceptible compartment.

Denoting by $s(t), e(t), i(t)$ and $r(t)$ the proportions of S, E, I and R in the total population of size $N(t)$ such that $s(t) + e(t) + i(t) + r(t) = 1$, the system in Equation 2.2 can be reduced to

$$\begin{aligned} \frac{ds}{dt} &= \lambda - \alpha(i+e) - \beta si - s\lambda \\ \frac{de}{dt} &= \beta si + \alpha(i+e) - \gamma e - e\lambda \\ \frac{di}{dt} &= \gamma e - \nu i - i\lambda \end{aligned} \qquad (2.3)$$

which is defined on the closed, positively invariant set $\Sigma = \{(s, e, i) \in \mathrm{R}_+^3 \mid 0 \leq s + e + i \leq 1\}$ (Korobeinikov, 2004). The system in Equation 2.3 has two equilibrium solutions for the proportion variables; the disease-free equilibrium state $Q_0 = (1,0,0)$ and the endemic equilibrium state $Q^* = (s^*, e^*, i^*)$, where

$$\begin{aligned} s^* &= \frac{(\lambda+\gamma)(\lambda+\nu)-\alpha(\lambda+\gamma+\nu)}{\beta\gamma} \\ e^* &= \frac{\lambda\beta\gamma+\alpha\lambda(\lambda+\gamma+\nu)-\lambda(\lambda+\gamma)(\lambda+\nu)}{\beta\gamma(\lambda+\gamma)} \\ i^* &= \frac{\lambda\beta\gamma+\alpha\lambda(\lambda+\gamma+\nu)-\lambda(\lambda+\gamma)(\lambda+\nu)}{\beta(\lambda+\gamma)(\lambda+\nu)} \end{aligned} \qquad (2.4)$$

In terms of the model parameters, the epidemiological threshold parameter of the model was defined by

$$R_0 = \frac{\beta\gamma+\alpha(\lambda+\gamma+\nu)}{(\lambda+\gamma)(\lambda+\nu)} \qquad (2.5)$$

The epidemiological threshold parameter. R_0, defines the expected number of secondary infections produced by a single infected individual introduced into the population. The increase or decrease in the spread of the disease is determined by whether $R_0 > 1$ or $R_0 < 1$ respectively (Cintrón-Arias et al., 2020). Based on R_0, the herd immunity threshold parameter, which is the critical proportion of the population needed to be immune to keep the disease under control, as defined by (Ashby and Best, 2021)

$$H = \frac{\beta\gamma+\alpha(\lambda+\gamma+\nu)-(\lambda+\gamma)(\lambda+\nu)}{\beta\gamma+\alpha(\lambda+\gamma+\nu)} \qquad (2.6)$$

2.2.1 Parameter estimation methodology

Let the observed cumulative incidence of HB in month i be represented by $Y_i = \sum_{j=1}^{i} y_j$, where $y_j, j = 1, \ldots, i$ is the observed incidence value at month j. The predicted cumulative incidence of HB is defined by (Cintrón-Arias et al., 2020)

$$h(t_i, \boldsymbol{\theta}) = \int_0^{t_i} \frac{\beta SI}{N} dt,\ i = 1,2,\dots,n.\ \boldsymbol{\theta} = (\beta, \gamma, \nu)$$

where t_i is the time in months and n is the total number of months. The parameter estimation procedure involved solving a nonlinear least squares problem

$$\min_{\boldsymbol{\theta} \in \mathbb{R}^3} [\sum_{i=1}^{n} [Y_i - h(t_i, \boldsymbol{\theta})]^2],\ \boldsymbol{\theta} = (\beta, \gamma, \nu) \geq \mathbf{0} \qquad (2.7)$$

where β, γ and ν are the model parameters to be estimated.

A hybrid method, which combined a Genetic Algorithm (GA) and a modified Levenberg Marquardt Algorithm (LMA), was used to solve this nonlinear least squares optimisation problem with MATLAB (version R2018a). The GA was applied first and started with a randomly generated population of candidate solutions $P = \{\boldsymbol{\theta}_z\}_{z=1}^{k}$, where k is the total population size. These solutions were coded as binary strings of Zeros $(0s)$ and Ones $(1s)$, which thevolved a progressively better population of solutions through crossover, mutation, migration and elimination. The GA provided a global search of the solution space to identify solutions that were assumed to be close to optimal. Following the GA, a modified LMA was applied to refine the solution generated by the GA. The LMA is a local gradient-based search method that does not include constraints. Thus, it was modified to account for the nonnegativity constraint. $\boldsymbol{\theta} = (\beta, \gamma, \nu) \geq \mathbf{0}$, in Equation 2.7. The standard LMA determines the solution to Equation 2.7 without the nonnegativity constraint $\boldsymbol{\theta} = (\beta, \gamma, \nu) > 0$, by solving iteratively

$$\left(J_{LM}^T J_{LM} + \lambda \text{diag}(J_{LM}^T J_{LM})\right)\boldsymbol{\delta}_i = J_{LM}^T [Y - h(\boldsymbol{\theta}_i)] \qquad (2.8)$$

where $Y = [Y_1, Y_2, \dots, Y_n]^T, h(\boldsymbol{\theta}) = [h(t_1, \boldsymbol{\theta}), h(t_2, \boldsymbol{\theta}), \dots, h(t_n, \boldsymbol{\theta})]^T$ and J_{LM} is the Jacobian matrix of $h(\boldsymbol{\theta})$ defined by $J_{LM} = \frac{\partial h(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}_i}$ (Gavin, 2019). Furthermore, the non-negativity constraint was achieved by projecting or rescaling the new solution of Equation 2.8 back onto the boundary whenever it falls outside the domain of interest (solution region), if the current solution initially was on the boundary or inside the solution region, respectively.

2.3 Stability analysis of model

To analyse stability of the model in the neighbourhood of the two equilibrium solutions for the proportion variables, the system in Equation 2.3 was linearised by constructing the Jacobian

$$J(s, e, i) = \begin{bmatrix} -(\beta i + \lambda) & -\alpha & -(\alpha + \beta s) \\ \beta i & \alpha - \lambda - \gamma & \alpha + \beta s \\ 0 & \gamma & -(\lambda + \nu) \end{bmatrix} \qquad (2.9)$$

whose eigenvalues at equilibrium solutions can be used to determine the stability of those solutions.

2.3.1 Disease-free equilibrium state

At the disease-free proportion equilibrium $Q_0 = (1,0,0)$, the eigenvalues were

$$\begin{aligned} \xi_1 &= -\lambda \\ \xi_2 &= \frac{(\alpha - \gamma - \nu - 2\lambda) + \sqrt{(\alpha + \nu - \gamma)^2 + 4\gamma(\alpha + \beta)}}{2} \\ \xi_3 &= \frac{(\alpha - \gamma - \nu - 2\lambda) - \sqrt{(\alpha + \nu - \gamma)^2 + 4\gamma(\alpha + \beta)}}{2} \end{aligned} \qquad (2.10)$$

Since the birth rate of babies with HB is less than overall birth rate of the population, $< \lambda$, it follows that $(\alpha - \gamma - \nu - 2\lambda) < 0$. Furthermore, since $\alpha, \beta, \gamma, \nu \geq 0$, it follows that $(\alpha + \nu - \gamma)^2 + 4\gamma(\alpha + \beta) > 0$, which implies that all eigenvalues are real and both $\xi_1, \xi_3 < 0$. However, If $\beta < ((\lambda + \nu - \alpha)(\gamma + \lambda) - \alpha\nu)/\gamma$, then $\xi_2 < 0$; If $\beta = ((\lambda + \nu - \alpha)(\gamma + \lambda) - \alpha\nu)/\gamma$, then $\xi_2 = 0$; and If $\beta > ((\lambda + \nu - \alpha)(\gamma + \lambda) - \alpha\nu)/\gamma$, then $\xi_2 > 0$. Hence there is a threshold value

$$\beta^* = \frac{(\lambda + \nu - \alpha)(\gamma + \lambda) - \alpha\nu}{\gamma} \qquad (2.11)$$

such that if $\beta < \beta^*, \xi_1, \xi_2, \xi_3 < 0$ and $Q_0 = (1,0,0)$ is locally asymptotically stable and if $\beta > \beta^*, \xi_1, \xi_3 < 0$ and $\xi_2 > 0$ so that $Q_0 = (1,0,0)$ is unstable (saddle)

Local stability of the disease-free proportion equilibrium Q_0 was established as equivalent to all the real parts of the eigenvalues of the Jacobian in Equation 2.9 being negative, which is guaranteed by the restriction $R_0 < 1$. The parameter restriction $R_0 < 1$ was used to discuss the global stability of the disease-free equilibrium Q_0 in Σ, in the sense of Lyapunov and LaSalle as given by the following theorems (Li et al., 1999).

Theorem 1 (LaSalle's Theorem) Let $\Omega \subset D \subset \mathbb{R}^n$ be a compact positively invariant set with respect to an autonomous system of equations $\dot{x} = f(x)$, $f(0) = x_0$. Let $V: D \to \mathbb{R}$ be a continuously differentiable function such that $\dot{V}(x(t)) \leq 0$ in Ω. Let $E \subset \Omega$ be the set of all points in Ω where $\dot{V}(x) = 0$. Let M $\subset$ E be the largest invariant set in E. Then every solution starting in Ω approaches M as $t \to \infty$, that is

$$\lim_{t\to\infty} \left(\underbrace{\inf_{z\in \mathrm{M}} ||x(t) - z||}_{dist(x(t),\mathrm{M})} \right) = 0.$$

A formal proof of this theorem can be found in (Shub, 2013). The inclusion of the sets in Theorem 1 then becomes $Q_0 \subset$ E $\subset \Sigma \subset \mathbb{R}^3_+ \subset \mathbb{R}^n$, leading to the following result.

Theorem 2 The disease-free equilibrium $Q_0 = (1,0.0)$ of the system in Equation 2.3 is globally asymptotically stable in $\sum$ if $R_0 \leq 1$.

Proof. Let $R_0 \leq 1$ and $V(s(t), e(t), i(t)) = \gamma e + (\lambda + \gamma - \alpha)i$, where $V: \mathbb{R}^3_+ \longrightarrow \mathbb{R}$ is a scalar function that is continuous and has continuous derivatives in $\mathbb{R}$. Differentiating V with respect to time t and using the system in Equation 2.3 where $\frac{de}{dt} = e'$ and $\frac{di}{dt} = i'$ gives

$$\begin{aligned} \dot{V}(s,e,i) &= \gamma e' + (\lambda + \gamma - \alpha)i' \\ &= \gamma[\beta s i + \alpha(i + \epsilon) - \gamma e - e\lambda] + (\lambda + \gamma - \alpha)[\gamma e - \nu i - i\lambda] \\ &= \gamma[(\beta s + \alpha)i - (\lambda + \gamma - \alpha)e] + (\lambda + \gamma - \alpha)[\gamma e - (\lambda + \nu)i] \\ &= i[\gamma\beta s + \alpha(\lambda + \gamma + \nu) - (\lambda + \gamma)(\lambda + \nu)] \end{aligned} \tag{2.12}$$

Using Equation 2.5. Equation 2.12 can be written in the form

$$\begin{aligned} \dot{V}(s,e,i) &= i\left[\frac{\gamma\beta s - \gamma\beta + \gamma\beta + \alpha(\lambda+\gamma+\nu) - (\lambda+\gamma)(\lambda+\nu)}{(\lambda+\gamma)(\lambda+\nu)}\right] \times \\ &\quad (\lambda + \gamma)(\lambda + \nu) \\ &= i\left[\frac{\gamma\beta s - \gamma\beta}{(\lambda+\gamma)(\lambda+\nu)} + \frac{\gamma\beta + \alpha(\lambda+\gamma+\nu)}{(\lambda+\gamma)(\lambda+\nu)} - 1\right](\lambda + \gamma)(\lambda + \nu) \end{aligned} \tag{2.13}$$

$$= i[\gamma\beta(s-1) + (R_0 - 1)(\lambda + \gamma)(\lambda + \nu)] \tag{2.14}$$

Since $R_0 \leq 1$ and $s \leq 1$ in Σ, it follows that $\gamma\beta(s-1) + (R_0 - 1)(\lambda + \gamma)(\lambda + \nu) \leq 0$. Hence for $i \geq 0$ in $\Sigma, \dot{V}(s,e,i) \leq 0, \forall (s,e,i) \in \Sigma$. Furthermore, $\dot{V} = 0$ if $i = 0$ or $\gamma\beta(s-1) + (R_0 - 1)(\lambda + \gamma)(\lambda + \nu) = 0$ and so $s = 1$ and $R_0 = 1$. But if $s = 1$, it follows that $i = 0$ which then implies that $\dot{V} = 0$ regardless of the value of R_0. The set $E = \{(s,e,i) \mid 0 \leq s + e \leq 1, i = 0\}$ is the set of all points in Σ where $\dot{V}(x) = 0$ and $\{Q_0\}$ is invariant, since $(s(0), e(0), i(0)) = Q_0$ implies $(s(t), e(t), i(t)) = Q_0, \forall t \in \mathbb{R}$. For any trajectory (s,e,i) starting in E to remain in E requires that $i' = 0$. However if $i = 0$, then from the third equation of Equation 2.3 that $i' = \gamma e$ so that $L = \{(s,e,i) \mid 0 \leq s \leq 1, i = e = 0\}$ is the only positively invariant part of E because the system in Equation 2.3 reduces to

$$s' = (1 - s)\lambda,\ e' = 0,\ i' = 0 \tag{2.15}$$

Thus, all trajectories (s,e,i) starting on the s-axis remain on the s-axis for $t \geq 0$ and, in fact, approach the singleton $\{Q_0\} \subset L \subset E$ as $t \longrightarrow \infty$. But for $t < 0$, all trajectories (s,e,i) starting in E move in the negative s-direction and ultimately fall outside of the closed positive set Σ as $t \longrightarrow -\infty$, thereby making the set L positively invariant. Thus the maximum invariant set in E is the singleton $\{Q_0\} \subset L \subset E \subset \Sigma$ and so $\lim_{t\to\infty} \mid (s,e,i) - Q_0 \parallel = 0$, which completes the proof.

2.3.2 Endemic equilibrium state

At the endemic proportion equilibriun state $Q^* = (s^*, e^*, i^*)$, the characteristic equation is of the form

$$\xi^3 + a_2\xi^2 + a_1\xi + a_0 = 0 \tag{2.16}$$

where

$$a_2 = \frac{(\lambda+\nu)(\gamma\nu+\lambda\nu+\gamma^2+2\lambda^2)+\gamma\lambda(3\lambda+\beta)+2\gamma\lambda\nu+\gamma\nu(\lambda-\alpha)}{(\gamma+\lambda)(\lambda+\nu)}$$
$$a_1 = \frac{\lambda(\alpha\gamma^2+\alpha\lambda^2+\beta\gamma^2+\alpha\nu^2+\beta\gamma\nu+\alpha\gamma\nu+2\alpha\gamma\lambda+2\beta\gamma\lambda+2\alpha\nu\lambda)}{(\lambda+\nu)(\gamma+\lambda)}$$
$$a_0 = \lambda(\beta\gamma+\alpha\nu)-\lambda(\lambda+\nu-\alpha)(\lambda+\gamma)$$

The general condition for a matrix A to be stable is when the real parts of all its eigenvalues are negative. In this study, however, the complexity of the coefficients a_0, a_1, and a_2 of the characteristic equation in Equation 2.16 rendered the search for eigenvalues of the endemic equilibrium state $Q^* = (s^*, e^*, i^*)$ practically impossible. Instead, stability of the endemic equilibrium state Q^* was discussed using the spectral properties of the second additive compound matrix $J^{[2]}$ of the Jacobian J of the system in Equation 2.3 (Li et al., 1999).

Considering the following, Lemma

Lemma 1 Let A be a $m \times m$ matrix with real entries. For A to be stable, it is necessary and sufficient that

(i) The second additive compound matrix A^2 of A is stable.

(ii) $(-1)^m \det(A) > 0$

the second additive compound matrix of the Jacobian $J(Q)$ in Equation 2.9 at the point $Q = (s, e, i)$ was derived as

$$J^{2]}(Q) = \begin{bmatrix} -2\lambda-\beta i-\gamma+\alpha & \alpha+\beta s & \alpha+\beta s \\ \gamma & -2\lambda-\nu-\beta i & -\alpha \\ 0 & \beta i & \alpha-2\lambda-\nu-\gamma \end{bmatrix} \quad (2.17)$$

Proof (Lemma 1). It requires to show that the Jacobian J in Equation 2.9 satisfies conditions (i) and (ii) of Lemma 1 with respect to the endemic equilibrium state $Q^* = (s^*, e^*, i^*)$. Choosing the diagonal matrix $D = \mathrm{diag}(i^*, e^*, s^*)$, the matrix $J^{[2](Q^*)}$ at the point $Q^* = (s^*, e^*, i^*)$ is similar to

$$DJ^{[2]}(Q^*)D^{-1} = \begin{bmatrix} -2\lambda-\beta i^*-\gamma+\alpha & \frac{i^*}{e^*}(\alpha+\beta s^*) & \frac{i^*\alpha}{s^*}+\beta i^* \\ \frac{e^*\gamma}{i^*} & -2\lambda-\nu-\beta i^* & -\frac{\alpha e^*}{s^*} \\ 0 & \frac{\beta i^* s^*}{e^*} & \alpha-2\lambda-\nu-\gamma \end{bmatrix} \quad (2.18)$$

Since the similarity property preserves eigenvalues of similar matrices, the matrix $J^{2}](Q^*)$ is stable if $D.J^{[2]}(Q^*)D^{-1}$ is stable and vice versa. The diagonal entries of the matrix $DJ^{[2]}(Q^*)D^{-1}$ are all negative since $\lambda > \alpha$. Hence by Geršgorin disc, $DJ^{[2]}(Q^*)D^{-1}$ is stable because its rows are diagonally dominant. The matrix $DJ^{[2]}(Q^*)D^{-1}$ is diagonally dominant when $\psi = \max\{r_1, r_2, r_3\} < 0$ where r_1, r_2, and r_3 are the sum rows 1,2 , and 3 respectively of the transformed Jacobian in Equation 2.18 given by

$$\begin{aligned} r_1 &= \alpha-\gamma-2\lambda+\frac{\alpha i^*}{s^*}+\frac{(\alpha+\beta s^*)i^*}{\epsilon^*} \\ r_2 &= \frac{\gamma e^*}{i^*}-2\lambda-\beta i^*-\nu-\frac{\alpha e^*}{s^*} \\ r_3 &= \frac{\beta i^* s^*}{e^*}+\alpha-\gamma-2\lambda-\nu \end{aligned} \quad (2.19)$$

By equating the system in Equation 2.3 to zero and rearranging gives

$$\begin{aligned} \frac{\lambda-\alpha(i^*+e^*)}{s^*} &= \beta i^*+\lambda \\ \frac{(\beta s^*+\alpha)i^*}{e^*} &= \gamma+\lambda-\alpha \\ \frac{\gamma e^*}{i^*} &= \nu+\lambda \end{aligned} \quad (2.20)$$

Substituting Equation 2.20 into Equation 2.19, the set ψ was derived to be

$$\psi = \mathrm{m}\left\{-\lambda+\frac{\alpha i^*}{s^*}, -\lambda-\frac{\alpha e^*}{s^*}-\beta i^*, -\lambda-\nu-\frac{\alpha i^*}{e^*}\right\} < 0$$

since $\lambda > \alpha$ and so $\frac{i^*}{s^*} < \frac{\lambda}{a}$. This satisfies condition (i) of Lemma 1 . Furthermore, using Equation 2.20

$$\det\left(J(Q^*)\right) = \begin{vmatrix} -\frac{\lambda-\alpha(i^*+e^*)}{s^*} & -\alpha & -\frac{e^*}{i^*}(\gamma+\lambda-\alpha) \\ \beta i & -\frac{i^*}{e^*}(\beta s^*+\alpha) & \alpha+\beta s \\ 0 & \gamma & -\frac{\gamma e^*}{i^*} \end{vmatrix} \quad (2.21)$$

$$= -\frac{\lambda-\alpha(i^*+\epsilon^*)}{s^*}[\gamma(\alpha+\beta s^*)-\gamma(\alpha+\beta s^*)] - \alpha\beta\gamma e^* \quad (2.22)$$

$$-\beta\gamma e^*(\lambda+\gamma-\alpha)$$

$$= -\alpha\beta\gamma e^* - \beta\gamma e^*(\lambda+\gamma-\alpha)$$

$$= -\beta\gamma e^*(\lambda+\gamma) < 0 \quad (2.23)$$

which satisfies condition (ii) of Lemma 1 and thus completes the proof.

2.3.3 Threshold stability point between Q_0 and Q

From Subsection 2.3.2, the coefficients for the characteristic equation of the Jacobian of the endemic equilibrium state Q^* were given as

$$a_2 = \frac{(\lambda+\nu)(\gamma\nu+\lambda\nu+\gamma^2+2\lambda^2)+\gamma\lambda(3\lambda+\beta)+2\gamma\lambda\nu+\gamma\nu(\lambda-\alpha)}{(\gamma+\lambda)(\lambda+\nu)}$$

$$a_1 = \frac{\lambda(\alpha\gamma^2+\alpha\lambda^2+\beta\gamma^2+\alpha\nu^2+\beta\gamma\nu+\alpha\gamma\nu+2\alpha\gamma\lambda+2\beta\gamma\lambda+2\alpha\nu\lambda)}{(\lambda+\nu)(\gamma+\lambda)}$$

$$a_0 = \lambda(\beta\gamma+\alpha\nu)-\lambda(\lambda+\nu-\alpha)(\lambda+\gamma)$$

Since $\alpha,\beta,\gamma,\lambda,\nu \geq 0$ and $\lambda > \alpha$, the coefficients a_2 and a_1 are positive, whilst $a_0 < 0$ if $\beta < \beta^*$: $a_0 > 0$ if $\beta > \beta^*$; and $a_0 = 0$ if $\beta = \beta^*$. From Descartes' rule of signs, it follows that the signs of the eigenvalues of the characteristic equation in Equation 2.16 are negative when $\beta > \beta^*$ so that Q^* is feasible and asymptotically stable but Q^* is infeasible and unstable when $\beta < \beta^*$ (Cheriha H, 2019). When $\beta = \beta^*$, the proportion equilibrium point is $(s^*, e^*, i^*) = (1,0,0)$ and

$$a_2 = \gamma-\alpha+3\lambda+\nu,\ a_1 = \lambda(\gamma-\alpha+2\lambda+\nu),\ a_0 = 0 \quad (2.24)$$

so that $\xi_1 = -\lambda < 0, \xi_2 = \alpha-\gamma-\nu-2\lambda < 0$ and $\xi_3 = 0$. Hence $\beta = \beta^*$ is a common threshold for stability crossover between the disease-free Q_0 and endemic Q^* proportion equilibrium states, when $Q^* = Q_0, a_0 = 0, R_0 = 1$, one eigenvalue $\xi_3 = 0$ and the remaining two are $\xi_1, \xi_2 < 0$. The disease-free state Q_0 is locally asymptotically stable for $\beta < \beta^*$ whilst the endemic state Q^* is locally asymptotically stable for $\beta > \beta^*$ with respect to the proportion variables.

2.3.4 Disease persistence

The dynamics of the system in Equation 2.3 in the domain Σ, was determined globally for $R_0 \leq 1$ by Theorems 1 and 2 . From an epidemiological perspective, this result implies that the total infected fraction of the population $e+i \longrightarrow 0$ as $t \longrightarrow \infty$ and so the disease tends to die out of the population. The contrast is when $R_0 > 1$ and the disease persists; for a sufficiently long time, the total infected fraction $e+i \longrightarrow$ of the population increases beyond a certain critical value. According to (Li et al., 1999).

Definition 1 The system in Equation 2.3 can be described as uniformly persistent if $\exists c. 0 < c < 1$ such that every solution $(s(t), e(t), i(t)) \in \sum^2$ starting from $(s(0), e(0), i(0)) \in \sum$ will satisfy the condition

$$\mathrm{m}\left\{\lim_{t\to\infty} \mathrm{i}\ [s(t)], \lim_{t\to\infty} \mathrm{i}\ [e(t))_{-2} \lim_{t\to\infty} \mathrm{i}\ [i(t)] \geq c\right.$$

From Theorem 1 and Definition 1 , let $\Omega = \Sigma, \Sigma \subset \mathbb{R}^3_+$, and $x = (s,e,i) \in \mathbb{R}^3_+$ be the component populations whose interactions were modelled by the system in Equation 2.3. The following proposition was made.

Proposition 1 If the the system in Equation 2.3 is uniformly persistent in Σ°, then $R_0 > 1$ and vice versa.

It was established in Subsection 2.3.3 of this study that exactly one of the equilibrium states was stable at any given time with respect to the dynamics of the system in Equation 2.3. In the absence of a periodic solution, the endemic equilibrium was the only attractor in Σ. In the setting of the system in Equation 2.3, it can be observed that the necessary and sufficient condition for uniform persistence is equivalent to the result that Q_0 is unstable which was determined in Subsection 2.3.3 to occur when $R_0 > 1$. From Theorem 2 and Proposition 1, R_0 was established to be the epidemiological threshold parameter of the system in Equation 2.3; if $R_0 \leq 1$ the disease is kept under control. or else $R_0 > 1$ and the disease uniformly persists in the population.

3. DISCUSSION OF RESULTS

An SEIR model incorporated proportionate mixing and varying population size in this study. Latent period and vertical transmission was applied to incidence data to examine the transmission and spread of HB in an endemic setting. The model was defined by a system of nonlinear ordinary differential equations. The entire dynamical behaviour of the model was determined based on the basic parameters that defined the system. The global behaviour of the model was discussed using the proportionate values (s, e, i), which also determined the behaviour of the absolute case (S, E, I). Hence disease eradication or persistence referred to the total infected proportions $(e + i)$ vanishing or uniformly persisting respectively in the population.

The epidemiological threshold parameter of the model was derived as $R_0 = (\beta\gamma + \alpha(\lambda + \gamma + \nu))/((\lambda + \gamma)(\lambda + \nu))$, where the total infected proportion tend to disappear when $R_0 \leq 1$ and otherwise tend to uniformly persist when $R_0 > 1$. Thus, the model has two equilibrium states: a disease-free state $Q_0 = (1,0,0)$ which is globally asymptotically stable when $R_0 \leq 1$ and the disease tend to die out, and an unique endemic state $Q^* = (s^*, e^*, i^*)$ which is asymptotically stable when $R_0 > 1$ and the disease persists. Stability crossover between the disease-free equilibrium state and endemic equilibrium state occurs at a threshold value $\beta^* = ((\lambda + \nu)\ \gamma)(\lambda + \gamma) - \alpha\nu)/\gamma$ of the contact rate when $R_0 = 1$; If the contact rate $\beta < \beta^*, R_0 < 1$ and so the disease-free equilibrium state is stable whilst the endemic equilibrium state is infeasible and unstable, and if $\beta > \beta^*$ the endemic equilibrium state is stable and the disease-free equilibrium state is unstable.

The SEIR model was applied to HB incidence data of an endemic country. By the hybrid optimization method described in Subsection 2.2.1, the parameters estimated for the model. based on the HB incidence data, were a contact rate $\beta = 0.0480$, a latent rate $\gamma = 0.1254$ and a recovery rate $\nu = 0$. Using Equation 2.1, the vertical transmission rate $\alpha = 0.0019$ was calculated based on the HB incidence data and natural birth rate $\lambda = 0.0249$. From these estimated parameters, the epidemiological threshold parameter $R_0 = 1.6854$ was calculated for the model. This value of $R_0 > 1$ indicated that HB persists in the population, which emphasises the need to take steps to control its transmission and spread. At this rate of persistence, a herd immunity threshold value $H = 0.4067$ was calculated which indicated the fraction of the population needed to be immune in order to keep the disease under control. The recovery rate $\nu = 0$ indicated that none of the infected persons, due to the dynamics of the disease, could clear the disease at the acute stage as supported by literature on HB. The rate $\nu = 0$ could also be due to numerical artefact in the estimation process or limitations in the HB incidence data used.

The model predicted the disease to stabilise at the endemic proportion equilibrium state value $Q^* = (0.5741, 0.0706, 0.3553)$, with time, where about $s = 57.4\%$ of the population are susceptible, $e = 7.1\%$ are exposed and $i = 35.5\%$ are infectious. Figure 9 displays the model prediction of the proportion variables s, e, and i with time. A latent period of about 7 months was calculated for the model, which provides a basis to conclude that latent period is not only important but significant in modelling HB. Numerical simulation using the estimated parameters. as baseline values, indicated that the epidemiological threshold parameter R_0 is most sensitive to vertical transmission rate α, compared with the contact rate β, latent rate γ and recovery rate ν. Figures $4 - 8$ display the simulation process analysing the sensitivity of the epidemiological threshold parameter R_0 with respect to each of the parameters $\alpha, \beta, \gamma, \nu$, and λ respectively.

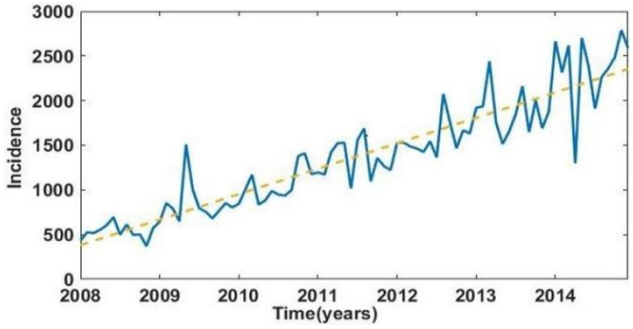

Figure 1: Time series plot of HB incidence data (2008-2014).

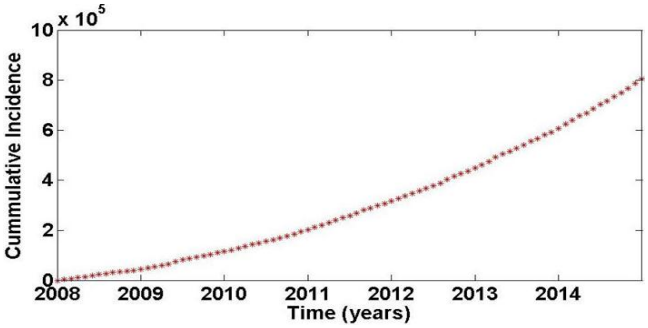

Figure 2: Cumulative incidence plot of HB incidence data (2008-2014).

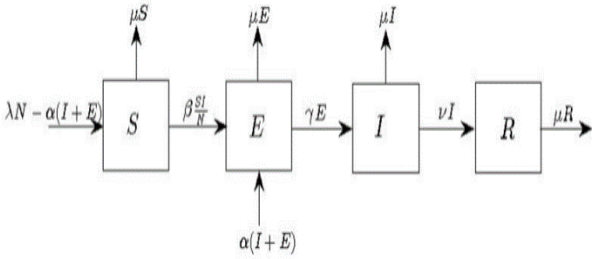

Figure 3: A model for transmission of HB.

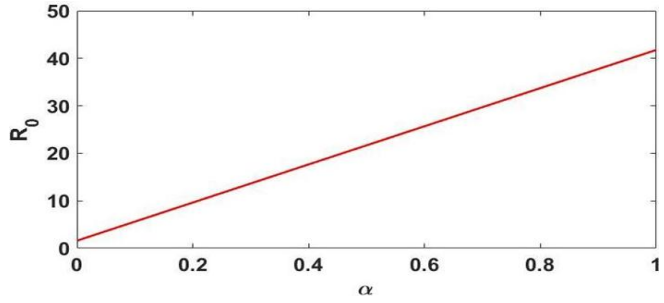

Figure 4: Sensitivity of R_0 to α.

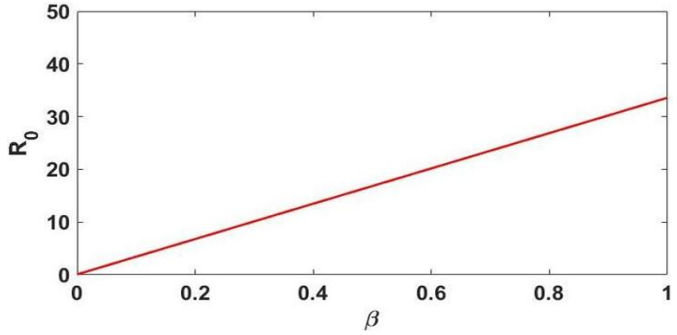

Figure 5: Sensitivity of R_0 to β.

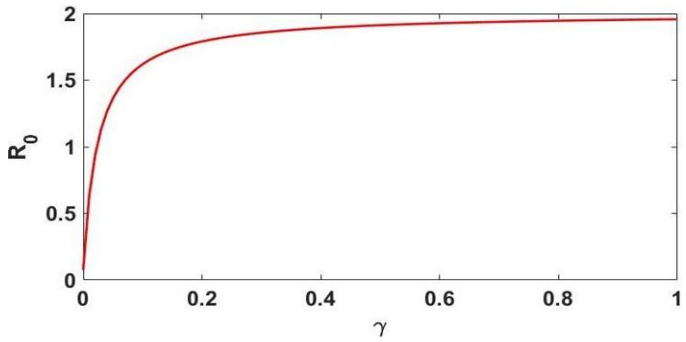

Figure 6: Sensitivity of R_0 to γ.

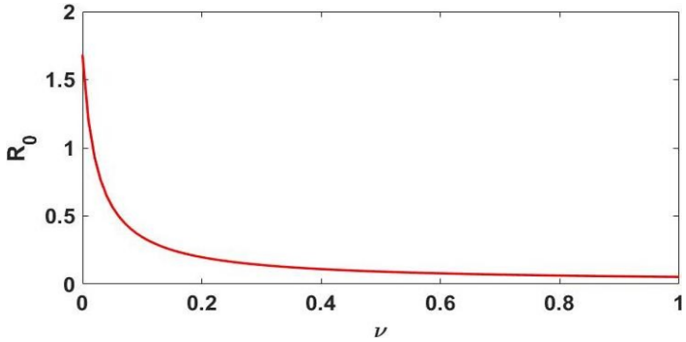

Figure 7: Sensitivity of R_0 to ν.

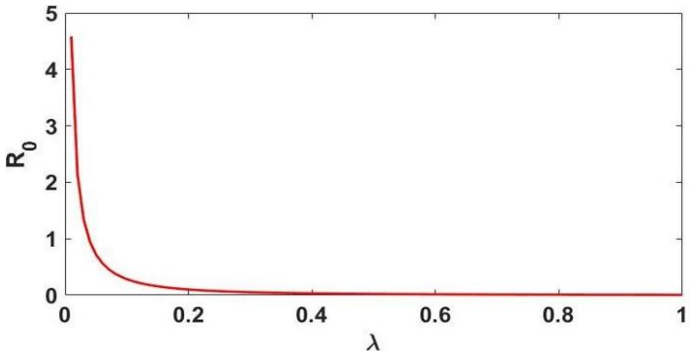

Figure 8: Sensitivity of R_0 to λ.

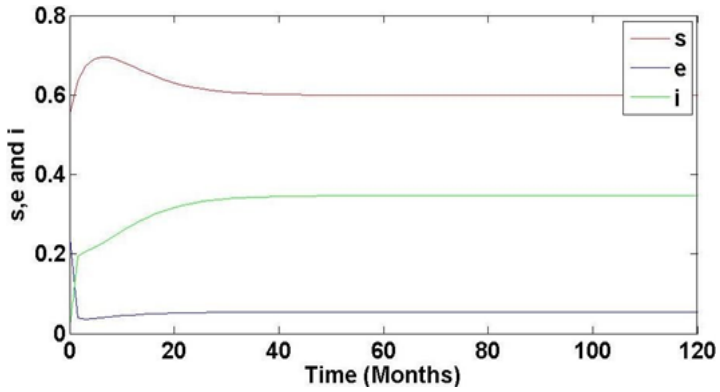

Figure 9: Model prediction of s, e and i with time.

3.1 CONCLUSION

An SEIR model incorporating vertical transmission, proportionate mixing, and varying population size was analysed concerning the transmission and spread of HB in an endemic setting. The model explicitly defined an epidemiological threshold parameter R_0, which when $R_0 < 1$ the disease-free state $Q_0 = (1,0,0)$ is globally asymptotically stable and the endemic state $Q^* = (s^*, e^*, i^*)$ is infeasible and unstable and so disease is kept under control in the population. When $R_0 > 1$ the disease-free Q_0 is unstable, an unique endemic state Q^* is asymptotically stable and the disease persists. Disease eradication or persistence meant the total infected proportion $(e + i)$ disappears or uniformly persists respectively. Applying the model to HB incidence data, a hybrid optimization method was used to estimate the parameters for contact rate $\beta = 0.0480$, latent rate $\gamma = 0.1254$, recovery rate $\nu = 0$, and based on these parameters, the epidemiological threshold parameter $R_0 = 1.6803$ was calculated. The value $R_0 = 1.6803 > 1$ indicates that the disease-free state Q_0 is unstable and the endemic state Q^* is stable and so HB persists in the population. The model predicted the disease to stabilise at the unique endemic equilibrium value $Q^* = (0.5741, 0.0706.0.3553)$ where about 57.4% of the total population are susceptible, 7.1% are exposed and 35.5% are infectious. This indicates that HB uniformly persists with total infected proportion 0.4259, representing about 43% of the population, which is alarming. Although transmission and spread of HB in the population was determined by all the parameters, stability of the model was most sensitive to vertical transmission rate (α). Vertical transmission therefore was found to be the major drive to the transmission and spread of HB in the population compared with the other parameters. It was found that achieving a herd immunity threshold value $H = 0.4067$, representing about 41% of the population would bring the disease under control. From the results of the study, the importance of latent period and contact rate in modelling HB cannot be overemphasised.

4. ACKNOWLEDGEMENT

The first author was supported by the ECUPRS International Postgraduate scholarship of Edith Cowan University, Western Australia. The hepatitis B incidence data and demographic data were provided by GHS and GSS respectively.

CONFLICT OF INTEREST

None.

REFERENCES

Aoudjane, S. et al. (2014). Hepatitis B virus sub-genotype A 1 infection is characterized by high replication levels and rapid emergence of drug resistance in HIV-positive adults receiving first-line antiretroviral therapy in Malawi. Clinical Infectious Diseases, 59: 1618 1626.

Ashby, B. and Best, A. (2021). Herd immunity. Current Biology, 31(4):R174-R 177.

CDCP (2016). Hepatitis b faqs for the public: Url=http://http://Www.cdc .gov/ hepatitis/hbv/bfaq.htm.

Cheriha H, Gati Y, K. V. P. (2019). A non-realization theorem in the context of descartes' rule of signs. arXiv preprint arXiv: 1911.12255.

Cintrón-Arias, A., Castillo-Chávez, C., Bettencourt, L. M.. Lloyd, A. L.. and Banks, H. (2020) .

The estimation of the effective reproductive number from disease outbreak data. arXiv preprint arXiv: 2004.06827.

Compston, L. I.. Li, C., Sarkodie, F.. Owusu-Ofori, S., Opare-Sem, O., and Allain. J.-P. (2009). Prevalence of persistent and latent viruses in untreated patients infected with hiv-1 from ghana, west africa. Journal of medical virology. 81(11): 18601868.

Dontwi, I., Obeng-Denteh, W., Obiri-Apraku, L., and Andam, E. (2014). Modelling Hepatitis B in a high prevalence district in Ghana. British Journal of Mathematics 8 Computer Science, 4(7): 969 − 988.

Gavin, H. P. (2019). The levenberg-marquardt algorithm for nonlinear least squares curve-fitting problems. Depaertment of Civil and Environmental Engineering, Duke University, 2(2):1-19.

Gentile I, B. G. (2014). Vertical transmission of hepatitis b virus: challenges and solutions. Int Journal of Women's Health, 6: 605 − 611.

GSS (2014). Ghana demographic and health survey, 2003. Ghana Statistical Service (Unpublished 9/12/2015)

Hawkins, C., Agbaji, O., Ugoagwu, P., Thio, C. L., Auwal, M. M.. Ani, C.. Okafo, C. Wallender. E., and Murphy, R. L. (2013). Assessment of liver fibrosis by transient elastography in patients with hiv and hepatitis b virus coinfection in nigeria. Clinical Infectious Diseases, 57(12): e189 e192

Korobeinikov, A. (2004). Lyapunov functions and global properties for seir and seis epidemic models. Mathematical Medicine and Biology, 21(2): 75 − 83.

Kramvis, A. and Kew, M. C. (2007). Epidemiology of hepatitis b virus in africa, its genotypes and clinical associations of genotypes. Hepatology Research. 37(s1). Li, M. Y.. Graef, J. R.. Wang, L., and Karsai, J. (1999). Global dynamics of a seir model with varying total population size. Mathematical biosciences, 160(2): 191213.

Locarnini, S., Littlejohn, M., Aziz, M. N., and Yuen, L. (2013). Possible origins and evolution of the Hepatitis B virus (HBV). In Seminars in cancer biology. volume 23, pages 561 − 575. Elsevier.

Ministry of health Ghana, M. (2014). Ghana national policy on viral hepatitis. Unpoblished. November 2014.

Nelson, K. E., Williams, C. M., Graham, N. M., and Balows, A. (2001). Infectious disease epidemiology theory & practice.

Ott, J. J., Stevens, G. A.. and Wiersma, S. T. (2012). The risk of perinatal hepatitis b virus transmission: hepatitis b e antigen (hbeag) prevalence estimates for all world regions. BMC infectious diseases, 12(1): 131

Shub, M. (2013). Global stability of dynamical systems. SIAM.

Smith, H. L.. Wang, L., and Li, M. Y. (2001). Global dynamics of an seir epidemic model with vertical transmission. SIAM Journal on Applied Mathematics, 62(1): 5869.

Van den Driessche, P. and Watmough, J. (2002). Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. Mathematical biosciences, 180(1): 29 − 48

Wearing, H. J.. Rohani, P., and Keeling, M. J. (2005). Appropriate models for the management of infectious diseases. PLoS medicine, 2(7): e174.

WHO (2016). Hepatitis b fact sheet: Url=http://http://www . who. int/mediacentre/ factsheets/fs 204/ en/.

WHO (2020). Global policy report on prevention and control of viral hepatitis: Url= htt : //www . who. int/news-room/factsheet/detail/hepatitis-b.

Wiktor, S. (2015). Where next for hepatitis b and c surveillance? Journal of viral hepatitis, 22(7): 571 − 573

Xin-zhu, M., Lan-sun, C., and Zhi-tao, S. (2007). Global dynamics behaviors for new delay seir epidemic disease model with vertical transmission and pulse vaccination. Applied Mathematics and Mechanics, 28(9): 12591271.