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MATHEMATICAL MODELLING AND SIMULATION OF MENINGOCOCCAL MENINGITIS TRANSMISSION DYNAMICS.

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ABSTRACT

Meningococcal meningitis disease remains a serious public heath challenge in the Meningitis belt. Despite series of measures taken to address the problem the disease often reoccurs at unpredicted times. This necessitates continuous research into the problem to find a lasting solution to the menace. Here, a deterministic model for the transmission dynamics of the disease with a variable total population is considered. The disease basic reproduction number $(\Re_0)$ is derived and the model equilibria are obtained. It is established that the disease free equilibrium is globally asymptotically stable whenever $\Re_0 < 1$. The model is solved numerically with Nigeria demographic data. Numerical simulations of our model results indicate that the prevalence and incidence of the disease both tend to zero for scenarios with $\Re_0 < 1$*;* this corroborates the conclusion from our analysis. Findings from our simulations also show that control measures which reduce the disease transmission rate and immunity waning rate as well as increase the vaccination and treatment success rate would be effective in eradicating Meningitis epidemic in the belt on the long-run.

Keywords: Meningococcal meningitis, Disease prevalence, Disease incidence, Global asymptotic stability, Basic reproduction number.

INTRODUCTION

Meningococcal meningitis is a bacterial form of meningitis that affects the thin lining surrounding the brain and the spinal cord. It could result into severe brain damage while it can also lead to death in 50% of untreated cases (WHO, 2017). Thus, it constitutes a serious public health problem, particularly, in the Meningitis belt of the sub-Saharan Africa. In this region, a lot of people become ill due to Meningitis infection every year and the epidemic spread across countries in the belt at frequent but unpredicted times causing several deaths. Consequently, there is the need for continuous research works on the disease transmission dynamics to be able to timely predict the recurrence of the epidemic and take pro-active measures that would minimize the casualties resulting from each outbreak.

Moreover, it is imperative to mention that the disease is transmitted from human-to-human through droplets of respiratory or throat secretions from carriers. Also, it may spread via prolonged contact or stay with carriers. Generally, about 10-20% of any given populations are carriers of the bacteria, though; the number of the carriers may increase to as high as 25% of the population

in epidemic situation (WHO, 2017). However, there are series of potent vaccines often deployed to prevent the spread of the disease in such circumstances. Though, the vaccine that would eventually be deployed would depend on the meningitis serogroup that is to be addressed, and possibly the cost of the vaccine.

There have been series of research works on modeling Meningitis transmission dynamics and its control (Trotter and Greenwood, 2007; Muller and Gessner, 2010; Martinez et al, 2013; Christensen et al, 2014; Elmojtaba and Adam, 2017; Asamoah et al, 2018; Yaesoubi et al, 2018). These works have different emphases and interests. For example, Vareen (2008) used an SCIR model to assess the impact of vaccination program on the spread of the disease in countries prone to meningitis epidemic. Their findings showed that in countries with high transmission rate, the vaccination rate should be scaled up appropriately to mitigate the alarming spread of the disease. Also, Blyuss (2016) used mathematical models to point out the crucial factors influencing the meningitis dynamics. Their results indicated that level of temporary immunity enjoyed by individuals in the community is very vital in disease surveillance and measuring vaccine efficiency.

In a related study, Martinez *et al* (2013) presented a novel model for the spread of Meningococcal meningitis which was based on cellular automata theory. The model was able to predict the global and the individual behavior of the disease while results from the simulations of the model agree with the empirical one in terms of the role played by the carriers in the disease transmission dynamics.

The rest of the paper is structured as follows: the proposed mathematical model will be presented with the justification that it is mathematically and epidemiologically well-posed. In the section that follows, the model will be qualitatively analyzed. Thereafter, the model will be solved numerically; it will be simulated for the different scenarios of interest and findings from our simulations will be discussed. Finally, in the last section, the conclusion from the study will be highlighted.

THE MATHEMATICAL MODEL

The Blyuss model for the transmission dynamics of Meningococcal meningitis is considered with some modifications (Blyuss, 2016). The model is modified by making the total population a variable; rather than being a constant as it is in the Blyuss model. This modification seems justifiable because the casualties recorded during the yearly Meningitis epidemic in the belt is substantial, thus affect the population thereafter (i.e. total population varies). In addition, the effect of vaccines deployed during epidemics is incorporated into the model dynamics, since this is often the practice in such instances to curtail the alarming spread of the disease. Obviously, these modifications will change the disease transmission dynamics significantly. Thus, an improved model with these modifications the Blyuss model is proposed. This model divides the total population N into four mutually exclusive compartments: the susceptible class S, the carrier class C, the infected class I , and the recovered cum temporarily immune class R where S, C, I, R represents the number of individuals in each of the compartments per unit time. Thus, $N(t) = S(t) + C(t) + I(t) + R(t)$. In the light of the foregoing, the proposed model is presented below:

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \frac{\beta S(C+I)}{N} - (\upsilon + \mu)S + \sigma R \\
\frac{dC}{dt} &= \frac{\beta S(C+I)}{N} - (\rho + \gamma + \mu)C \\
\frac{dI}{dt} &= \rho C - (\varepsilon + \delta + \mu)I \\
\frac{dR}{dt} &= \upsilon S + \gamma C + \varepsilon C - (\sigma + \mu)R
\end{aligned} \qquad (1)$$

Where Λ is the average recruitment rate, β is the disease transmission rate, υ is the vaccination *rate*, σ is the immunity waning rate, ρ is the carriers' disease progression rate , γ is their recovery rate, ε is the infected individuals treatment success rate, δ is the disease-induced death rate, while μ is taken to be human's natural death rate.

Since our model depicts human population dynamics; all the variables and parameters are non-negative. Consequently, a biological feasible region defined below is considered:

$$\Omega = \left\{ (S, C, I, R) \in \Re_+^4 : N \le \frac{\Lambda}{\mu} \right\} \qquad (2)$$

Nevertheless, there is the need to establish that the region Ω is positive invariant; which implies that all solution in Ω remains in it for all time t. In order to establish this, the summation of all the model equations in (1) yields:

$$\frac{dN}{dt} = \Lambda - \mu N - \delta I \le \Lambda - \mu N \qquad (3)$$

The inequality equation emanating from equation (3) is

$$\frac{dN}{dt} \le \Lambda - \mu N \qquad (4)$$

Solving equation (4) gives:

$$N(t) \le N(0)e^{-\mu t} + \frac{\Lambda}{\mu}(1 - e^{-\mu t})$$

where $N(0)$ is the initial total population at the start time.

In particular, $N(t) \le \frac{\Lambda}{\mu}$ whenever $N(0) \le \frac{\Lambda}{\mu}$.

So, every solution of our model equations (1) with initial conditions in Ω remains there for all time $t > 0$. Therefore, Ω is positive invariant? As a result, our model can be said to be mathematically and epidemiologically well-posed.

MODEL QUALITATIVE ANALYSIS

The model has two equilibria: the Disease–free equilibrium and the Endemic equilibrium. These equilibria are obtained by setting the right-hand side of each of the equations in (1) to zero and solving for each of the variables.

So, the model equilibria are obtained as below:

i. Disease-free equilibrium, E_0 : $E_0 = \left(\frac{\Lambda(\sigma+\mu)}{\mu(\nu+\sigma+\mu)}, 0, 0, \frac{\Lambda\nu}{\mu(\nu+\sigma+\mu)} \right)$.

ii. Endemic Equilibrium, E_1 - : $E_1 = \left(S^*, C^*, I^*, R^*\right)$ where

$$S^* = \frac{\Lambda\mu_2\mu_3(\mu_3\mu_4 + \mu_3\gamma + \rho\mu_4 + \rho\varepsilon)}{D}, \quad C^* = \frac{\Lambda\mu_3^{\,2}\mu_2(\mu_4+\nu)(\Re_0 - 1)}{D},$$

$$I^* = \frac{\Lambda\rho\mu_2\mu_3(\mu_4+\nu)(\Re_0 - 1)}{D}, \quad R^* = \frac{\Lambda[(\mu_3+\rho)(\mu_2\mu_3\nu + \beta(\mu_3\gamma + \rho\varepsilon)) - \mu_2\mu_3(\mu_3\gamma + \rho\varepsilon)]}{D}$$

with

$$D = \mu_2\mu_3\left[\mu_1\mu_3(\mu_4+\gamma) + \mu_1\rho(\mu_4+\varepsilon) + \mu_3\sigma(\gamma+\varepsilon) + \mu_4\beta(\mu_3+\rho)\right] - \beta\sigma(\mu_3+\rho)(\mu_3\gamma+\rho\varepsilon)$$
$$- \mu_2\mu_3\left[\mu_2\mu_3(\mu_4+\nu) + \nu\sigma(\mu_3+\rho)\right];$$

$$\mu_1 = \mu + \nu; \quad \mu_2 = \mu + \rho + \gamma; \quad \mu_3 = \mu + \varepsilon + \delta; \quad \mu_4 = \mu + \sigma.$$

While the basic reproduction number($\Re_0$) is computed using the Next-Generation-Matrix approach (Driessche and Watmough, 2002) and it is as expressed below:

$$\Re_0 = \frac{\beta(\sigma+\mu)}{(\nu+\sigma+\mu)(\rho+\gamma+\mu)} + \frac{\beta\rho(\sigma+\mu)}{(\nu+\sigma+\mu)(\rho+\gamma+\mu)(\varepsilon+\mu+\delta)}$$

$\Re_0$ is simply the average number of new cases of the disease arising from a single infected individual when introduced into a population where everyone is susceptible (Hethcote, 2000).

Theorem 1: The disease-free equilibrium, E_0, is globally asymptotically stable (GAS) whenever $\Re_0 < 1$.

Proof:

Considering a Lyapunov function V(t) of the form below :

$V = k_1C + k_2I$ *where* $k_1 > 0$ *and* $k_2 > 0$.

Then, differentiating the Lyapunov function with respect to t and substituting the model equations for C' *and* I' *gives:*

$$\begin{aligned} V' &= k_1C' + k_2I' \\ &= k_1\left[\frac{\beta S(C+I)}{N} - (\rho+\gamma+\mu)C\right] + k_2\left[\rho C - (\varepsilon+\mu+\delta)I\right] \\ &= \left[k_1\frac{\beta S}{N} + k_2\rho - k_1(\rho+\gamma+\mu)\right]C + \left[k_1\frac{\beta S}{N} - k_2(\varepsilon+\mu+\delta)\right]I \end{aligned}$$

Now, substituting the value of the S and R at the disease-free equilibrium E_0 yields:

$$V' \le \left[k_1\frac{\beta(\sigma+\mu)}{(\nu+\sigma+\mu)} + k_2\rho - k_1(\rho+\gamma+\mu)\right]C + \left[k_1\frac{\beta(\sigma+\mu)}{(\nu+\sigma+\mu)} - k_2(\varepsilon+\mu+\delta)\right]I.$$

Taking $k_1 = \frac{1}{\rho+\gamma+\mu}$, *and* $k_2 = \frac{\beta(\sigma+\mu)}{(\nu+\sigma+\mu)(\rho+\gamma+\mu)(\varepsilon+\mu+\delta)}$, *gives*

$$V' \leq \left[\frac{\beta(\sigma+\mu)}{(\nu+\sigma+\mu)(\rho+\gamma+\mu)} + \frac{\beta(\sigma+\mu)\rho}{(\nu+\sigma+\mu)(\rho+\gamma+\mu)(\varepsilon+\mu+\delta)} - 1\right]C,$$
$$\leq [\Re_0 - 1]C$$

Since $C \geq 0$ *for all time t, then* $V' \leq 0$ *if* $\Re_0 < 1$. *Moreover, it is imperative to note that for scenarios with* $\Re_0 < 1$ *as* $t \to \infty$, $(S, C, I, R) \to \left(\frac{\Lambda(\sigma+\mu)}{\mu(\nu+\sigma+\mu)}, 0, 0, \frac{\Lambda\nu}{\mu(\nu+\sigma+\mu)}\right)$. *Thus, based on LaSalle's invariance principle (Lasalle, 1976), every solution of the model equations (1) with initial condition in* Ω *converges to* E_0 *whenever* $\Re_0 < 1$. *Therefore, the disease-free equilibrium is globally asymptotically stable if* $\Re_0 < 1$.

NUMERICAL RESULTS AND DISCUSSION

Model Parameter values and Variables Initial Conditions:

The recruitment per unit time (Λ) into the susceptible population was estimated using the annual increase in the Nigeria's population from year 2000-2015. The Nigeria's average annual population increase is estimated to be 3.922 million per year (United Nation, 2017).

The life expectancy of a male Nigerian is 53 years while that of the female is 56 years (WHO, 2017). So, it is assumed that 0.5(53+56) = 54.5 years is the average life expectancy of a Nigerian at birth. Thus, the natural death rate is estimated as $d = \frac{1}{54.5} = 0.018\ yr^{-1}$.

Information from the World Health Organization has it that the disease is fatal in 50% of untreated cases, hence the disease induced death rate (δ) is taken to be 0.5 (WHO, 2017).

Also, it is known that there is an effective treatment for meningitis; thus it is assumed that a patient who undergoes early treatment has 50% chance of successfully getting rid of the bacteria. Hence, the disease treatment success rate (ε) is taken to be 0.5 (i.e. $\varepsilon = 0.5$) .

However, for the other remaining parameter values, the data from the works of Blyuss

(2016) and Irving *et al* (2012) were adopted. Below is a table of the model parameters with their respective values and their sources:

Table 1: Model parameter values.

Parameter	Value	Source
Λ	3.922	United Nation (2017) and Estimate
β	2.5	Estimate
ν	0.2	Estimate
μ	0.018	WHO (2017) and Estimate
σ	0.1	Irving et al (2012) and Blyuss (2016)
ρ	0.8	Irving et al (2012) and Blyuss (2016)
ε	0.5	Estimate
δ	0.5	WHO (2016) and Estimate
γ	0.25	Estimate

As for the model variables initial conditions, the Nigeria's demographic data for the year 2015 is adopted. The country total population for that year is 182 million (United Nation, 2017). The information that 10-20% of every population is carrier of Meningitis is used (WHO, 2017), so the average which is 15% is adopted as the case in Nigeria. This gives a carrier population of about 27.3 million. In addition, it is assumed that the population in each of infected and the recovered class is about one-third of those in carrier class. Thus, the model variables initial conditions are: $S(0)=136.5$, $C(0)=27.3$, $H(0)=9.1$, $R(0)=9.1$.

Simulation results and Discussion

The model equations (1) are solved numerically using Runge-Kunta of order four scheme and the results are simulated with the Maple software. In order to achieve this, the parameters values in Table 1 are used with the model variables' initial conditions: $S(0)=136.5$, $C(0)=27.3$, $H(0)=9.1$, $R(0)=9.1$.

It is important to state here that the set of parameters values in Table 1 yields a basic reproduction number greater than unity ($\Re_0=1.55$) which implies that the situation being considered is an endemic one. There is, therefore, the need to put effective control measures in place in order to minimize the attendant casualties that might results from the ensuing epidemic. First, the population profiles for each of the compartments are displayed in Figures 1- 4.

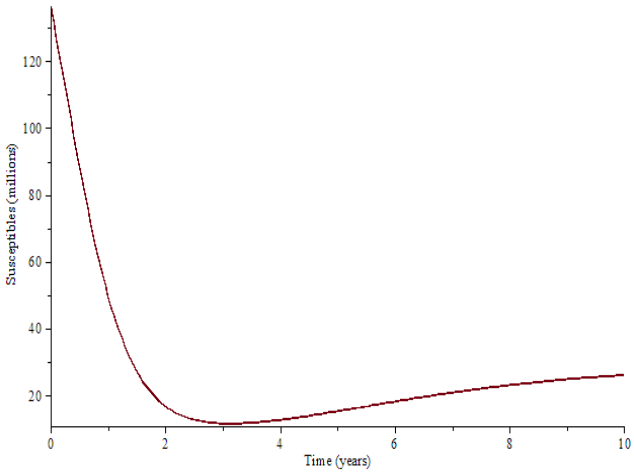

Figure 1: Population profile of S(t).

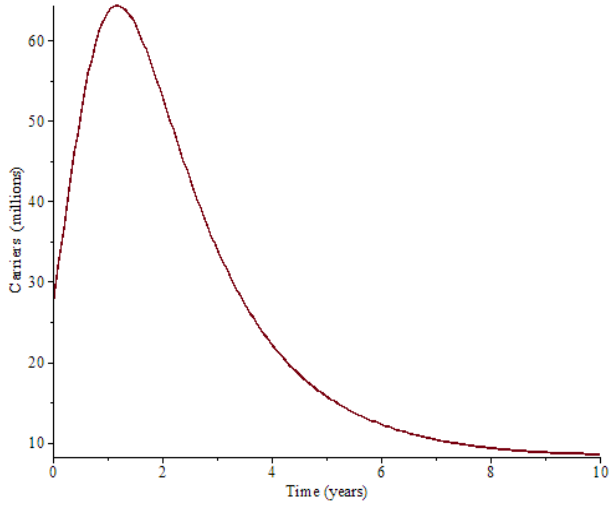

Figure 2: Population profile of C(t).

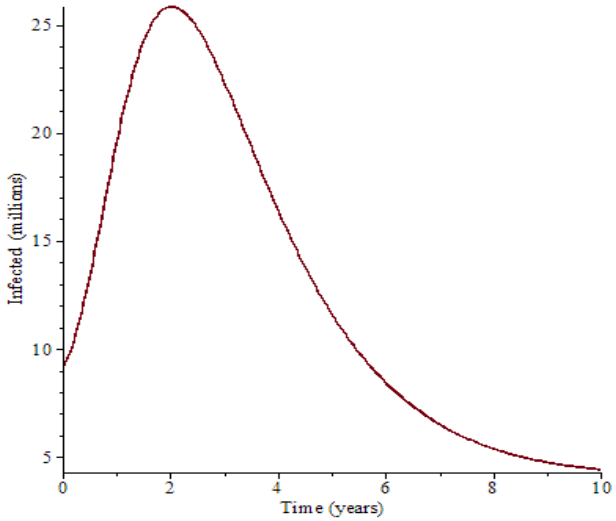

Figure 3: Population profile of I(t).

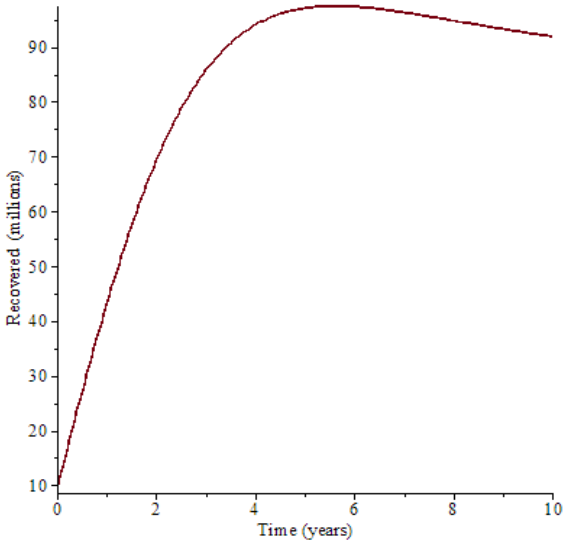

Figure 4: Population profile of R(t).

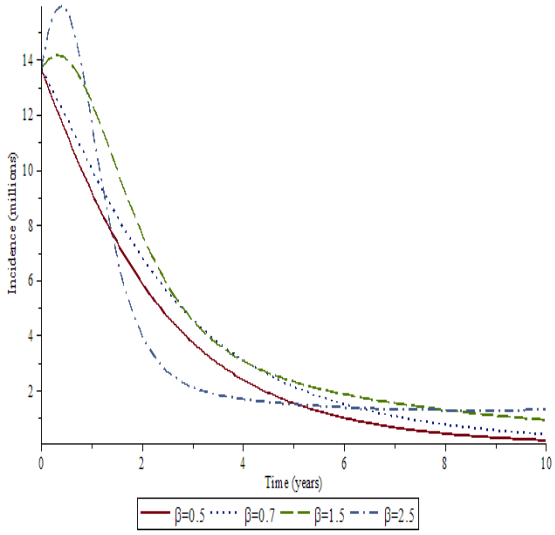

Figure 5: New Cases of Disease for different values of β .

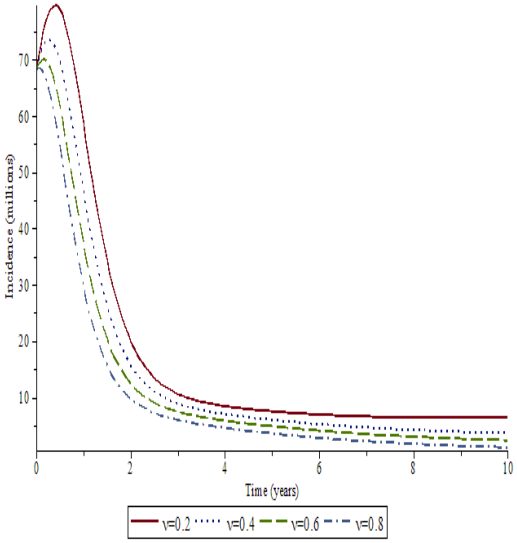

Figure 7: New Cases of Disease for different values of ν .

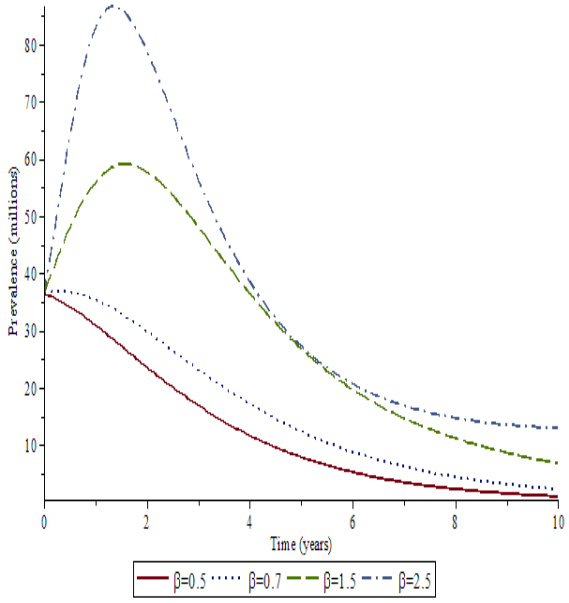

Figure 6: Prevalence of Disease for different values of β .

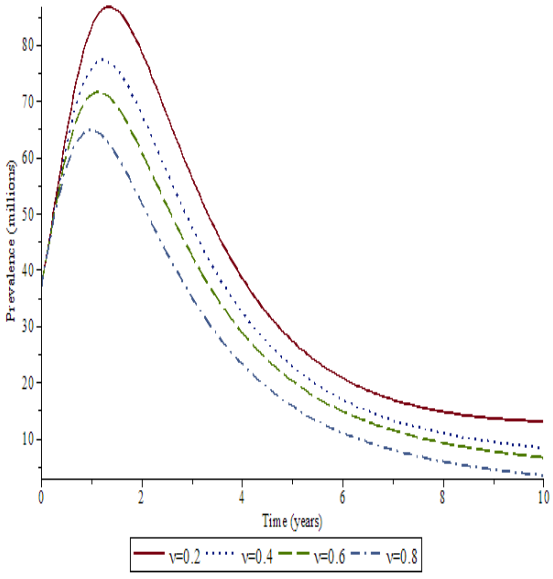

Figure 8: Prevalence of Disease for different values of ν .

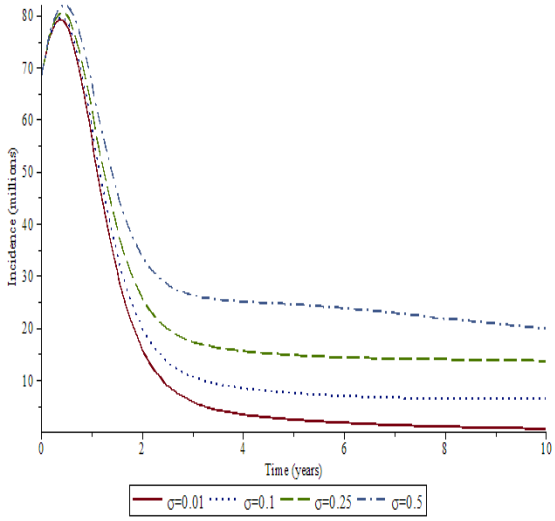

Figure 9: New Cases of Disease for different values of σ.

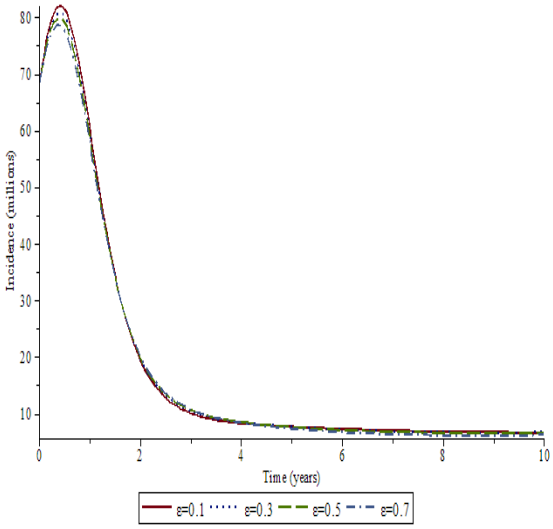

Figure 11: New Cases of Disease for different values of ε.

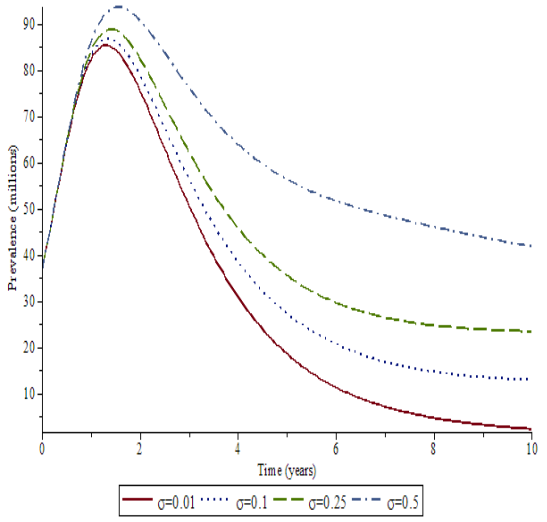

Figure 10: Prevalence of Disease for different values of σ.

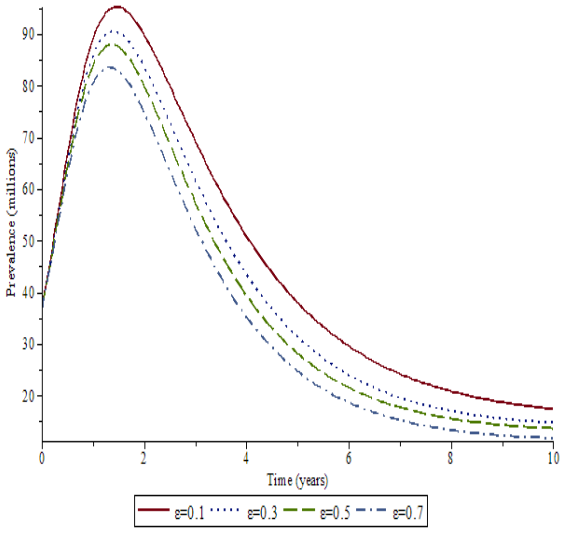

Figure 12: Prevalence of the Disease for different values of ε.

Results from the simulations of our model show that the new cases of the disease was at peak when the disease transmission rate was highest, while the peak attained in each of the scenario increases with increase in the transmission rate (See Fig. 5). However, it is salient to note that the first two scenarios in Figure 5 correspond to the situations where $\Re_0 < 1.0$ while the last two scenarios correspond to the situation where $\Re_0 > 1.0$. It is observed that for scenarios where $\Re_0 > 1.0$, there will always be new cases of the disease; unlike when $\Re_0 < 1.0$ where the

number of new cases tend to zero as time progresses. Also, Fig. 6 shows that the prevalence of the disease increases with increase in the disease transmission rate. Similarly, the prevalence of the disease tends towards extinction for situations with $\Re_0 < 1.0$. This corroborates the conclusion from theorem 1.

In addition, Figures 7 – 12 show that the incidence and prevalence of the disease fall as the vaccination rate, and treatment success rate increases. This implies that with the implementation of control measures that can enhance each of these factors, the incidence and prevalence of the disease could be significantly reduced. On the contrary, the incidence and prevalence of the disease falls as the immunity waning rate decreases. The implication of this is that any control measure that can elongate the temporary immunity duration would be useful in the control of the epidemic. In generally, any control measure that can reduce the basic reproduction number below unity would eventually lead to the eradication of the disease, on the long run.

The foregoing could be accomplished, if a continuous holistic enlightenment on Meningitis is done in each of the country in the Meningitis belt, so that individuals in that belt can take proactive steps to prevent themselves from getting infected while infected individuals present themselves for treatment as early as possible in order to forestall infecting more susceptible individuals. Nevertheless, regular and periodic vaccination of individuals in the belt should be embarked upon. This should be done such that individuals are re-vaccinated before the immunity enjoyed due to previous vaccine uptake wanes while vaccination coverage should be scaled up appropriately to confer herd immunity on each of the country in the belt.

CONCLUSION

In this paper, a deterministic model for Meningococcal meningitis transmission dynamics with variable total population size was considered. The model basic reproduction number and its equilibrium solutions were obtained. It was shown analytically and demonstrated numerically that the disease can be eradicated if effective control measures are put in place to drive the disease basic reproduction number below unity. Our simulation results show that control measures that can reduce the disease transmission rate and immunity waning rate as well as boost the vaccination rate and the treatment success rate would be effective in containing and possibly eradicating the meningitis epidemic.

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