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Effect of loss of vaccine induced immunity in the transmission dynamics of childhood disease

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Abstract
In this paper, a deterministic nonlinear model for the transmission dynamics of childhood disease is formulated and rigorously analyzed to explore the effect of loss of vaccine-induced immunity.
The model was shown to exhibit two equilibria, namely, disease free equilibrium and an endemic equilibrium and their local stability was established using the computated effective reproduction number (R_V). *The disease free equilibrium is globally asymptotically stable whenever* R_V *is less than unity by using an appropriate Lyapunov function. The global asymptotic stability of endemic equilibrium was established whenever* R_V *exceeds one by constructing a Lyapunov function using suitable combination of composite quadratic and logarithmic functions. Numerical simulation was done to validate its satisfactory agreement with the qualitative results, revealing that the loss of vaccine-induced immunity may be harmful to the spread of childhood disease provided it exceeds it critical threshold.*

Keywords: *Childhood diseases, Mathematical model, Lyapunov function, Threshold Analysis*

1.0 Introduction

In recent years, infectious diseases has taken the attention of vast numbers of individual, public health agency, government and non-government organization due to its devastating impact on public health and imposed great financial burden on the affecting communities (Akinyemi et al., 2016; Sahu and Dhar, 2015). The most common form of infectious diseases are childhood diseases which include chicken pox (also called varicella), rubella, measles, mumps, poliomyelitis, etc. Children within the age of 5 and below are more prone to these diseases due to their frequent contact with their peers, at school or other place (Cui et al., 2014). In 1980, it was recorded that about 2.6million individuals died of measles each year (World Health Organisation, 2013). Although, tremendous effort were made to develop vaccines in preventing childhood diseases. These vaccines were considered to be the most effective strategy in combating the spread of these diseases (Makinde, 2007). Meanwhile Peralta-Rodrigues et al., 2015, stated that despite the substantial reduction of morbidity, new cases of varicella infection were recorded mostly in highly vaccinated school communities after the implementation of the universal varicella vaccination program in the USA in 1955. Various studies of these cases have suggested that the predictors of immunity loss such as the time since vaccination and vaccination of new born may be associated with the persistence of varicella (Peralta-Rodrigues et al., 2015

and other references cited there in). Thus it becomes crucial to study the effect of loss of vaccine-induced immunity in the transmission dynamics of childhood diseases.

In scientific literatures, the use of mathematical models to investigate the transmission dynamics of infectious diseases has aroused the interest of Applied Mathematicians and Biologist. (Al-Sheik et al., 2011; Dogon and Akin, 2012). Several epidemic models for the transmission dynamics of childhood disease are found in (Moghadas and Gumel, 2003; Makinde,2007; Yildirim and Cherruault, 2009; Ibrahim and Ismail,2012; Cui, et al., 2014;El-Shahed and El-Naby,2014), although loss of vaccine-induced immunity and disease induced death were not considered. Epidemic models for childhood disease will be more realistic for developing countries when disease induced death rate are considered,examples of such are found in (Ochoche and Gweryina, 2014; Stephen et al., 2015) while SVIR model with loss of vaccine-induced immunity are found in (Peralta-Rodrigues et al., 2015). Hence this paper is concern with the formulation and rigorous analysis of a chidhood epidemic model with loss of vaccine-induced immunity with the aim of extending and complementing the one presented in (Makinde,2007; Ibrahim and Ismail, 2012; Cui, et al., 2014).

The paper is organized as follows. Section 2 presents the model formulation. In Section 3, equilibrium states, stability and threshold analysis of the model are presented while Section 4 presents numerical simulation and discussion of results. Section 5 concludes the paper.

2.0 Model Formulation

A non-linear deterministic model for the transmission dynamics of childhood disease in the presence of loss of vaccine induced immunity and constant vaccination is built by dividing the total human population at time t, denoted by $N(t)$ into three disjoint epidemiological subpopulations, which are the susceptible population $S(t)$, infected population $I(t)$ and the removed population $R(t)$ representing the population of both vaccinated and recovered individuals.

Thus $N(t)=S(t)+I(t)+R(t)$. (1)

The following assumptions were considered to construct the model

1. Individuals are only recruited into the susceptible and removed group.
2. The studied population varies with time and is homogenous.
3. Birth rate is not equal to death rate.
4. The force of infection is expressed as $\beta S(t)I(t)$.
5. The induced death rate of childhood disease was incorporated

The model is therefore governed by the following system of non-linear differential equations.

$$\frac{dS}{dt}=(1-P)\pi N-\frac{\beta SI}{N}-\mu S+\theta R$$
$$\frac{dI}{dt}=\frac{\beta SI}{N}-(\mu+\gamma+\delta)I$$
$$\frac{dR}{dt}=P\pi N+\gamma I-(\mu+\theta)R \quad (2)$$

The non-dimensional form of system (2) is given by:

$$\frac{ds}{dt} = (1-P)\pi - \beta si - \pi s + \theta r$$

$$\frac{di}{dt} = \beta si - K_1 i$$

$$\frac{dr}{dt} = P\pi + \gamma i - K_2 r$$

(3)

Where $s = \frac{S}{N}$, $i = \frac{I}{N}$, $r = \frac{R}{N}$, $K_1 = \pi + \gamma + \delta$, $K_2 = \pi + \theta$ and $n = s + i + r$

Table 1: Parameters Description and Hypothetical Values

Parameters	Symbols	Hypothetical Values	Source
Recruitment rate	π	0.4	Makinde,2007
Disease transmission coefficient	β	0.8	Ibrahim and Ismail,2012
Natural death rate	μ	0.02	Safiel et al., 2012; Ibrahim et al., 2015.
Disease induced death rate	δ	0.09	Rahman and Zou, 2012.
Recovery rate	γ	0.03	Makinde, 2007
Vaccination rate of newborn	P	$(0,1)$	Ibrahim and Ismail,2012
Rate of loss of vaccine-induced immunity	θ	$(0,1)$	Assumed

Lemma 1: The close set $\Omega = \{(s,i,r) \in \mathbb{R}^3_+ : s+i+r \le 1\}$ is positively invariant and attracting with respect to the system (3)

Proof

From (3), we note that $\frac{dn}{dt} = \pi - \pi n - \delta i \le \pi - \pi n$ and establish that $n(t) \le n(0)e^{-\pi t} + \left[1 - e^{-\pi t}\right]$ by a standard comparism theorem (Lakshmikantham et al., 1989). $n(t)$ approaches 1 as $t \to \infty$, so the system (3) is positively-invariant and attracting in Ω.Thus the model is mathematically and epidemiologically meaningful in Ω (Hethcote,2000), and it is sufficient to consider solutions in Ω.

3.0 Existence of Equilibrium States, Stability and Threshold Analysis

The disease free equilibrium of system (3) is obtained as

$$\varepsilon_0 = (S_*, i_*, r_*) = \left(\frac{K_2(1-P)+\theta P}{K_2}, 0, \frac{P\pi}{K_2}\right)$$

The effective reproduction number denoted by R_V will be used to analyze the stability of the model at ε_0. This is determine by using the next generation method as shown in (Heffernan et al., 2005), where F and V are matrices denoting the new infection terms and transition terms at ε_0 respectively. Therefore

$$F = \begin{pmatrix} \beta s & 0 \\ 0 & 0 \end{pmatrix} \qquad V = \begin{pmatrix} K_1 & 0 \\ -\gamma & K_2 \end{pmatrix}$$

$$R_V = \rho\left(FV^{-1}\right) = \frac{\beta\left(K_2(1-P)+\theta P\right)}{K_1K_2}$$

(4)

The endemic equilibrium of the model denoted by $\varepsilon_1 = \left(S^*, i^*, r^*\right)$ expressed in terms of R_V, is obtained as

$$\varepsilon_1 = \left(S^*, i^*, r^*\right) = \left(\frac{K_1}{\beta}, \frac{K_1K_2\pi\left(R_V-1\right)}{\beta\left(K_1K_2-\theta\gamma\right)}, \frac{P\pi+\gamma i^*}{K_2}\right)$$

(5)

3.1 Local Stability Analysis of Equilibrium States

Theorem 1: The disease-free equilibrium of system (3) is locally asymptotically stable whenever $R_V < 1$ and unstable otherwise.

Proof

The Jacobian matrix of the system (3), evaluated at ε_0 is given as

$$J\left(\varepsilon_0\right) = \begin{pmatrix} -\pi & -\beta s & \theta \\ 0 & \beta s - K_1 & 0 \\ 0 & \gamma & -K_2 \end{pmatrix}$$

(6)

The characteristic equation of (6) is of the form

$$\left(\lambda+\pi\right)\left(\lambda^2 + a_1\lambda + a_0\right) = 0$$

(7)

where

$a_1 = K_2 + K_1 - \beta s_*$

$a_0 = K_2\left(K_1 - \beta s_*\right)$

Expressing a_1 and a_0 in terms of R_V, with the aid of (4) to have

$a_1 = K_2 + K_1\left(1-R_V\right)$

$a_0 = K_1K_2\left(1-R_V\right)$

It is obvious that the roots of (7) are all negative whenever $R_V < 1$. Thus by Routh Hurwitz criterion, we conclude that the system (3) is locally asymptotically stable if and only if $R_V < 1$.

The epidemiological implication of Theorem 1 is that the spread of childhood disease can be effectively controlled in the community (when $R_V < 1$) if the initial sizes of the sub-populations of the model are in the basin of attraction of the disease-free equilibrium ε_0, otherwise the disease will continue to persist.

Theorem 2: The endemic equilibrium of system (3) is locally asymptotically stable whenever $R_V > 1$ and unstable otherwise.

Proof

The Jacobian matrix of the system (3), evaluated at ε_1 is given as

$$J(\varepsilon_1)=\begin{pmatrix} -\pi-\beta s & -\beta s & \theta \\ \beta i & \beta s-K_1 & 0 \\ 0 & \gamma & -K_2 \end{pmatrix}$$

(8)

The characteristic equation of (8) is of the form

$$\left(\lambda^3+b_2\lambda^2+b_1\lambda+b_0\right)=0$$

(9)

where

$$b_2=K_2+K_1+\pi+\beta i^*-\beta s^*$$

$$b_1=K_1K_2+K_2\pi+K_2\beta i^*-K_2\beta s^*+K_1\beta i^*+K_1\pi-\beta s^*\pi$$

$$b_0=K_1K_2\pi-\gamma\theta\beta i^*+K_1K_2\beta i^*-K_2\beta s^*\pi$$

Rewriting b_2, b_1 and b_0 in terms of R_V, using (4) to have

$$b_2=K_2+\pi+\beta i^*$$

$$b_1=K_2\pi+K_2\beta i+K_1\beta i^*$$

$$b_0=\beta i^*\left(K_1K_2-\gamma\theta\right)$$

Since the components of the endemic equilibrium are positive provided $R_V>1$, then b_2, b_1 and b_0 are greater than zero. Hence concluding the proof since Routh Hurwitz criterion is satisfied.

3.2 Global Stability Analysis of Equilibrium States

To qualitatively show that the dynamic behavior of the system is independent of the initial sizes of the sub population, global stability analysis is done by constructing suitable lyapunov function. Thus establishing the following results.

Theorem 4: The disease-free equilibrium of system (3) is globally asymptotically stable whenever $R_V<1$ and unstable otherwise.

Proof. Consider the Lyapunov function

$$L_1=i$$

(10)

Differentiating (10) with respect to time t to obtain

$$\frac{dL_1}{dt}=\frac{di}{dt}$$

Thus, using the second equation from system (3) to obtained

$$\frac{dL_1}{dt}=\beta si-K_1 i$$

(11)

Substituting $s\le s_*=\dfrac{K_2(1-P)+\theta P}{K_2}$ into (11), to get

$$\frac{dL_1}{dt}\le\left(\beta\frac{K_2(1-P)+\theta P}{K_2}-K_1\right)i$$

$$\frac{dL_1}{dt} \le K_1\left(\beta\frac{K_2(1-P)+\theta P}{K_1K_2}-1\right)i$$

$$\frac{dL_1}{dt} \le K_1(R_V-1)i$$

Clearly, $\frac{dL_1}{dt}\le 0$ when $R_V \le 1$ and $\frac{dL_1}{dt}=0$ if and only if $i=0$. It follows from Lasalle's Invariance Principle (La Salle and Lefschetz, 1961), that every solution to the system (3) with initial conditions in Ω approaches ε_0 as $t\to\infty$. Thus, since the region Ω is positively-invariant, the disease free equilibrium is globally asymtotically stable in Ω if $R_V \le 1$.

Theorem 4: The endemic equilibrium of system (1) is globally asymptotically stable whenever $R_V > 1$ and unstable otherwise.

Proof. Consider the Lyapunov function

$$L_2 = \frac{1}{2}\left(\left(s-s^*\right)+\left(i-i^*\right)+\left(r-r^*\right)\right)^2+\frac{2\pi+\delta}{\beta}\left(i-i^*-i^*In\frac{i}{i^*}\right)+\frac{(2\pi+\delta)}{2\gamma}\left(r-r^*\right)^2 \quad (12)$$

Differentiating (12) with respect to time to obtain

$$\frac{dL_2}{dt} = \left(\left(s-s^*\right)+\left(i-i^*\right)+\left(r-r^*\right)\right)\frac{dn}{dt}+\frac{2\pi+\delta}{\beta}\left(1-\frac{i^*}{i}\right)\frac{di}{dt}+\frac{(2\pi+\delta)}{2\gamma}\left(r-r^*\right)\frac{dr}{dt}$$

$$\frac{dL_2}{dt} = \left(\left(s-s^*\right)+\left(i-i^*\right)+\left(r-r^*\right)\right)\left(\pi-\pi(s+r)-(\mu+\delta)i\right)+\frac{2\pi+\delta}{\beta}\left(1-\frac{i^*}{i}\right)\left(\beta si-K_1i\right)+ \quad (13)$$

$$+\frac{(2\pi+\delta)}{2\gamma}\left(r-r^*\right)\left(P\pi+\gamma i-K_2r\right)$$

Using $\pi=\mu\left(s^*+r^*\right)+(\mu+\delta)i^*$ and $K_1=\beta s^*$ to simplify (13) as

$$\frac{dL_2}{dt} = -\left(\left(s-s^*\right)+\left(i-i^*\right)+\left(r-r^*\right)\right)\left(\pi\left(\left(s-s^*\right)+\left(r-r^*\right)\right)+(\pi+\delta)\left(i-i^*\right)\right)+(2\pi+\delta)\left(i-i^*\right)\left(s-s^*\right)$$

$$+\frac{2\pi+\delta}{\gamma}\left(r-r^*\right)\left(\gamma\left(i-i^*\right)-K_2\left(r-r^*\right)\right)$$

$$\frac{dL_2}{dt} = -\left(\left(s-s^*\right)+\left(r-r^*\right)\right)^2-(2\pi+\delta)\left(i-i^*\right)\left(\left(s-s^*\right)+\left(r-r^*\right)\right)-(\pi+\delta)\left(i-i^*\right)^2+$$

$$(2\pi+\delta)\left(i-i^*\right)\left(s-s^*\right)+\frac{2\pi+\delta}{\gamma}\left(r-r^*\right)\left(\gamma\left(i-i^*\right)-K_2\left(r-r^*\right)\right)$$

$$\frac{dL_2}{dt} = -\left(\left(s-s^*\right)+\left(r-r^*\right)\right)^2-(\pi+\delta)\left(i-i^*\right)^2-\frac{K_2(2\pi+\delta)}{\gamma}\left(r-r^*\right)^2$$

Thus, for $R_V>1, \frac{dL_2}{dt}\le 0$, where $\frac{dL_2}{dt}=0$ holds only when $s=s^*, i=i^*$ and $r=r^*$. The only largest invariant set in $\left\{(s,i,r)\in\Omega:\frac{dL_2}{dt}=0\right\}$ is the endemic equilibrium. Therefore the endemic

equilibrium ε_1 is globally asymptotically stable in the interior Ω, by LaSalle's invariance theorem principle (La Salle and Lefschetz, 1961).

3.3 Threshold Analysis and Critical Thresholds

To measure the effect of vaccination and loss of vaccine-induced immunity qualitatively, we perform threshold analysis. This is done by computing the partial derivatives of R_V with respect to P and θ respectively to obtain

$$\frac{\partial R_V}{\partial P} = \frac{-\beta\pi}{K_1 K_2} < 0 \tag{14}$$

$$\frac{\partial R_V}{\partial \theta} = \frac{\beta\pi P}{K_1 K_2^2} > 0 \tag{15}$$

We have from (14) that R_V is a decreasing function of P, thus increase in P will reduces R_V and consequently reduces the burden of childhood disease. Similarly, we note from (15) that R_V is an increasing function of θ, which signifies that childhood disease will continue to persist as θ increases.

The need to obtain critical threshold for P and θ is of great importance in eliminating or containing the spread of childhood disease. Thus we have from (4) the critical thresholds for vaccination and loss of vaccine-induced immunity denoted by P_C and θ_C respectively as

$$P_C = \frac{K_2(\beta - K_1)}{\beta\pi} \tag{16}$$

$$\theta_C = \frac{\pi\left(K_1 - \beta(1-P)\right)}{\beta - K_1} \tag{17}$$

It is readily seen by Theorem 1—4 that the following results hold true.

Theorem 5: The disease free equilibrium of system (3) is globally asymptotically stable whenever $P_C < P$ and unstable otherwise.

Theorem 6: The endemic equilibrium of system (1) is globally asymptotically stable whenever $\theta > \theta_C$ and unstable otherwise.

4.0 Numerical Simulation and Discussion

In this section, some numerical solutions of the model for different initial population sizes is presented using the various values of the parameters stated in Table.1 and to validate that these solutions are in agreement with the qualitative behaviors of the model obtained in section 2. Thus, we choose different initial population sizes such that the total population, $s+i+r=1$ as follows.

Table 2: Effect of vaccination at different parameter values $(P_C = 0.3938)$

s_0	i_0	r_0	θ	P	R_V	Remarks
1	0	0	0.05	0.9	0.3077	ε_0 stable (disease eradication)
0.8	0.2	0	0.05	0.9	0.3077	ε_0 stable (disease eradication)
0.8	0.2	0	0.05	0.3	1.1282	ε_1 stable (no eradication)
0.7	0.2	0.1	0.05	0	1.5385	ε_1 stable (no eradication)

Note: The table is generated by using the parameter values in Table 1

Table 3: Effect of loss of vaccine-induced immunity at different parameter values $(\theta_C = 0.0114)$

s_0	i_0	r_0	θ	P	R_V	Remarks
1	0	0	0	0.36	0.9846	ε_0 stable (disease eradication)
0.8	0.2	0	0.01	0.36	0.9981	ε_0 stable (disease eradication)
0.8	0.2	0	0.03	0.36	1.0233	ε_1 stable (no eradication)
0.7	0.2	0.1	0.05	0.36	1.0462	ε_1 stable (no eradication)

Note: The table is generated by using the parameter values in Table 1.

Fig.1 depict the numerical solution curve of the system (3) for $\theta = 0.05,\ P = 0.9, P_C = 0.3938$ and $R_V = 0.3077$, showing the impact of high vaccination coverage on the initial total population that is completely susceptible. The population of susceptible group decreases while the removed group increases with time. The total population remains at disease free equilibrium, since the infected group stays at zero at all time. Thus elimination of childhood disease is achievable whenever $P_C < P$ or $R_V < 1$ and the disease free equilibrium is globally stable.

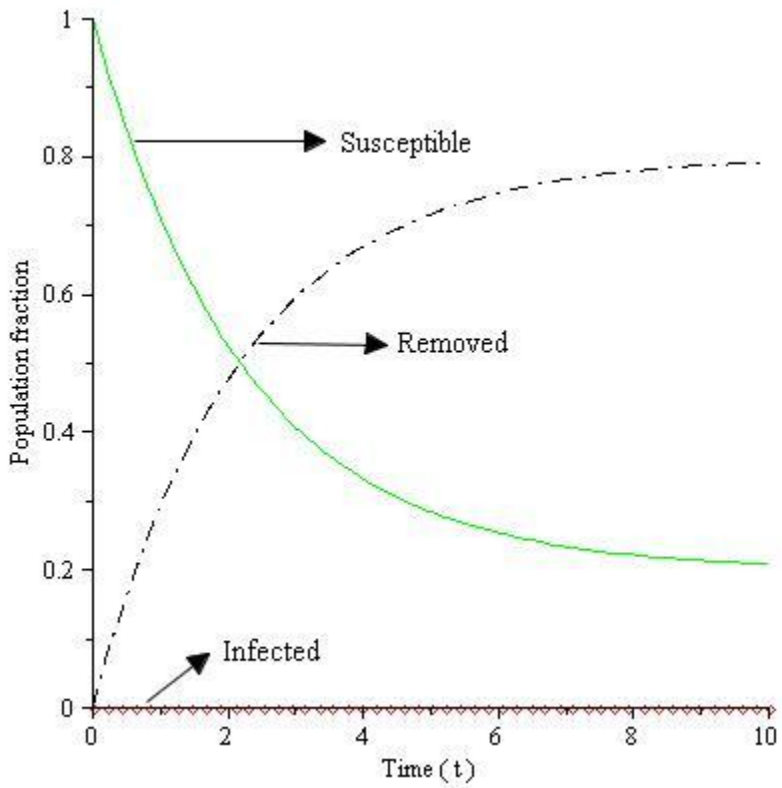

Fig. 1. Time plots of system (3) with different initial conditions for $R_v < 1$ (i.e. $P_C < P$)

Fig.2 depict the numerical solution curve of the system (3) for $\theta = 0.05,\ P = 0.3, P_C = 0.3938$ and $R_V = 1.1282$, showing the impact of low vaccination coverage on the initial population groups with a small population of infected individuals. The population of susceptible individuals decreases at first and slightly increases while the population of removed individuals increases with time. The population of infected individuals gradually decreases and will never tend to zero. Thus childhood disease will continue to persist whenever $P_C > P$ or $R_v > 1$ and the endemic equilibrium remains stable globally.

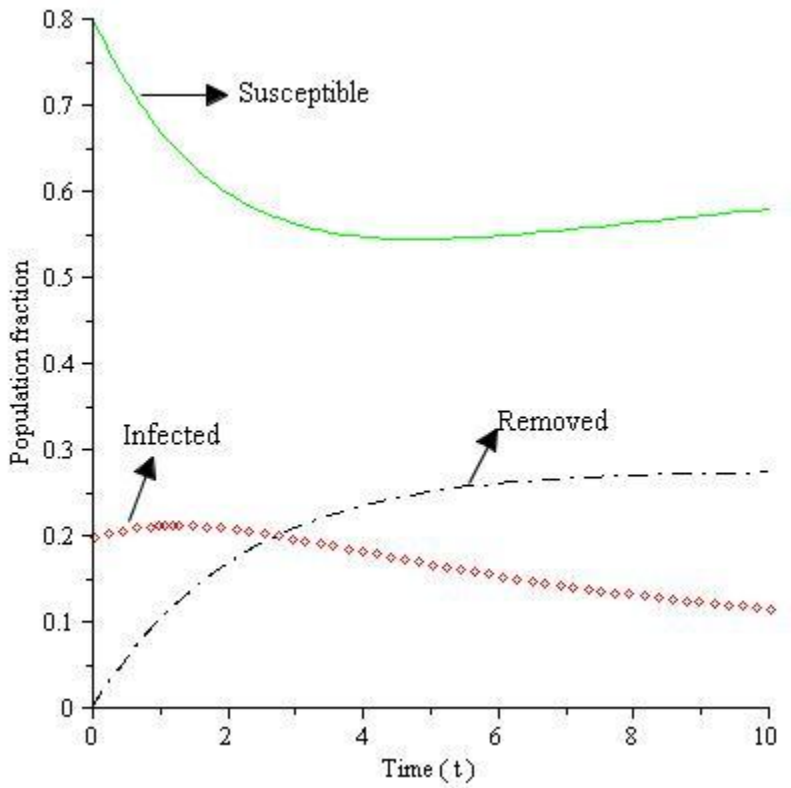

Fig. 2. Time plots of system (3) with different initial conditions for $R_v > 1$ (i.e. $P_C > P$)

Fig.3 shows the numerical solution curve of the system (3) for $P = 0.36$, $\theta = 0$, $\theta_C = 0.0114$ and $R_V = 0.9846$, displaying the impact of absence immunity loss on the disease free initial population groups. The population of susceptible individuals decreases while the population of removed individuals increases with time. The total population remains at disease free equilibrium, since the population of infected individual stays at zero at all time. The population of infected individuals gradually decreases and will never tend to zero. Thus whenever $\theta < \theta_C$ or $R_V < 1$, childhood disease will go into extinction and the disease free equilibrium is stable globally.

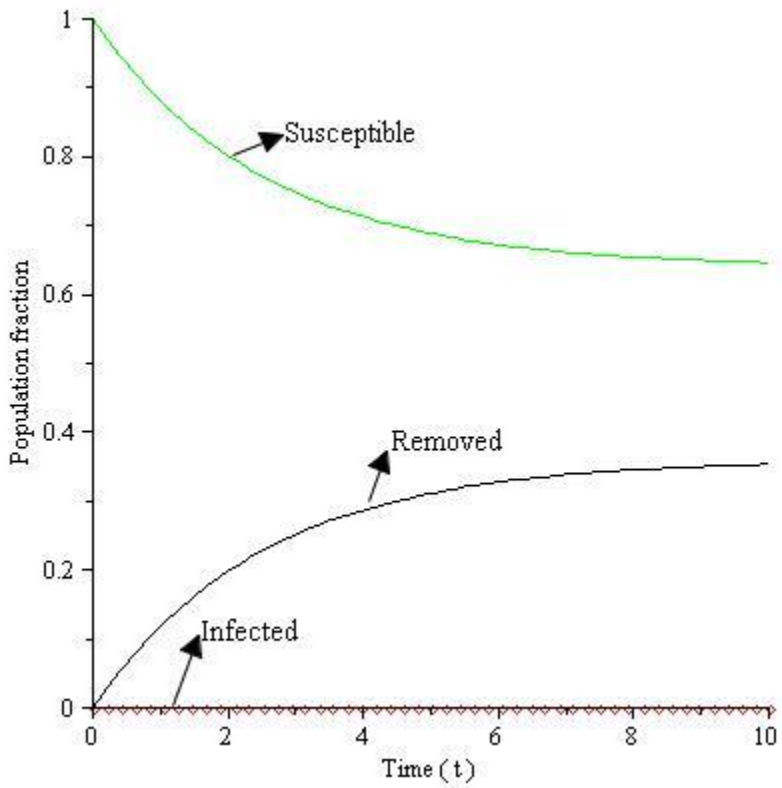

Fig. 3. Time plots of system (3) with different initial conditions for $R_v < 1$ (i.e. $\theta < \theta_C$)

Fig.4 shows the numerical solution curve of the system (3) for $P = 0.36$, $\theta = 0.03$, $\theta_C = 0.0114$ and $R_V = 1.0233$, displaying the impact of immunity loss on the initial population groups with a small population of infected individuals. The population of susceptible individuals decreases while the population of removed individuals increases with time. The population of infected individuals gradually decreases and will never tend to zero. Thus childhood disease will continue to persist whenever $\theta > \theta_C$ or $R_v > 1$ and the endemic equilibrium remains stable globally.

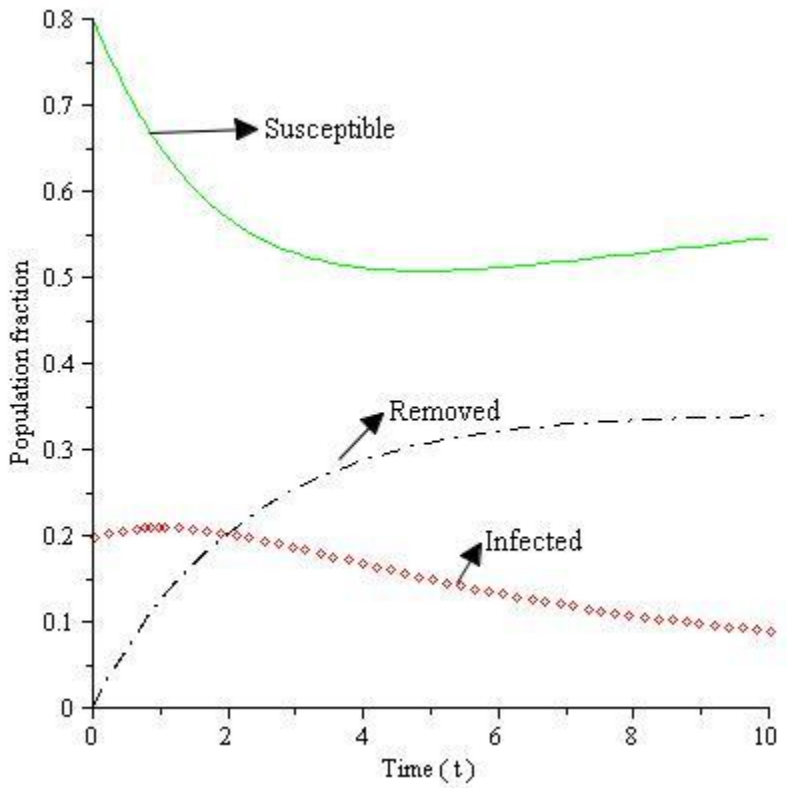

Fig. 4. Time plots of system (3) with different initial conditions for $R_v > 1$ (i.e. $\theta_C > \theta$)

5.0 Conclusion

In this paper, the epidemiological dynamics of childhood disease in the presence of loss of vaccine-induced immunity and constant vaccination was studied by formulating and analyzing a nonlinear model of three compartments. Some of the key findings are summarized as follows.

1. The model is globally-asymptotically stable at disease free equilibrium whenever the effective reproduction number R_V is less than unity.
2. The model's endemic equilibrium is globally asymptotically stable whenever the effective reproduction number exceeds unity.
3. An increase in vaccination coverage reduces effective reproduction number and consequently reduces prevalence of childhood disease. Thus elimination of childhood disease is achievable by increasing vaccination coverage above the critical vaccination threshold.
4. Higher level of loss of vaccine-induced immunity results in increase in effective reproduction number, and, hence aggrandizes the burden of childhood disease. Loss of vaccine-induced immunity is detrimental whenever it exceeds it critical threshold.

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