Effects of Hand Washing Campaign on Dynamical Model of Hand Foot Mouth Disease

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***Abstract*—In this study, we proposed a nonlinear mathematical model of Hand Foot Mouth Disease (HFMD) due to the effectiveness of hand washing campaign as a control strategy. The model is analyzed using stability theory of differential equations and computer simulation. The results showed that there were two equilibrium points; disease free equilibrium and endemic equilibrium point. The qualitative results depend on the basic reproductive number (R_0). We obtained the basic reproductive number by using the next generation method. Stabilities of the model are determined by Routh - Hurwitz criteria. If $R_0 < 1$, then the disease free equilibrium point is local asymptotically stable, but If $R_0 > 1$, then the endemic equilibrium point is local asymptotically stable. The graphical representations are provided to qualitatively support the analytical results. It concluded that with an increase in the effectiveness of hand washing campaign, the infected population reduced.**

***Index Terms*—Hand foot mouth disease, hand washing campaign, basic reproductive number, stability analysis, equilibrium point.**

I. Introduction

Hand Foot Mouth Disease (HFMD) is a common infectious disease that affects infants and children. HFMD is caused by an Enterovirus genus of Piconoviridae family [1]. The most common viruses causing HFMD are Coxsackievirus A16 (COX A16) and Enterovirus71 (EV71)[2]. Symptoms of HFMD is usually onset a fever, poor appetite, malaise, and sore throat. After fever starts, painful sores can develop in the mouth. The skin rush with flat or raised red spots can develop on the palms of the hands and soles of the feet and sometimes on the buttocks. Although, HFMD is a moderate contagious and not a serious illness among population [3]. There is no specific treatment or vaccine for HFMD. Therefore, the control measures of HFMD are based on appropriate prevention measure include quarantine mechanisms and personal protection against exposure to infected persons [4]. In Asia, HFMD is occurred in many countries; Malasia (1997 and 2006), Taiwan(1998), China(2008, 2009 and 2010), Singapore(2008), Vietnam (2008) and Mongolia(2008), Bruni(2008),Indonesia(2009) and Thailand(1958 and 2008) [3].

Mathematical models have become an important tool for understanding the spread and control of disease. Reference [3]. proposed a simple SEIR model for HFMD among the young children. The aim of this study to understand the dynamics of HFMD. The model was analyzed for analytic results and numerical simulation results. The results shown that disease transmission depends on the number of actively infected human at the initial time and also on the disease transmission coefficient at the given time. Reference [4] proposed an epidemic model of HFMD with periodic transmission rate. HFMD model was analyzed and investigated the effects of quarantine in children population. We obtain a threshold value which determines the extinction and uniform persistence of the disease. The results show that disease free equilibrium is global asymptotically stable if the threshold value is less than one. Otherwise, the system has a positive periodic solution and disease persist. The simulation results show that quarantine is beneficial intervention to control for this disease. Reference [5] proposed a mathematical model of HFMD to understand the dynamics and analyze the effectiveness of quarantine as a control strategy. The results show that disease could be control by quarantine of more actively infected individuals. The qualitative results show that disease transmission depends more on the number of actively infected at the initial time and also on the disease transmission coefficient at a given time. Reference [6] proposed a dynamic model with periodic transmission rates to investigate the seasonal HFMD. We obtain the basic reproductive number, analyze the dynamical behavior of the model and simulate the HFMD of Shandong Province. By carrying out the sensitivity analysis of some key parameters, we conclude that the recessive subpopulation plays an important role in the spread of HFMD.

The objective of the study is to determine the effectiveness of hand washing campaign as a control strategy on the dynamical transmission of HFMD model. The remainder of the paper is organized as follows. In Section II, we formulate the propose model. In Section III, we analyze the model by using stability theory of differential equations, to determine both disease free and endemic equilibrium point, derive the basic reproductive number and investigate the stability of the model. In Section IV, we simulate the numerical results, which confirm our theoretical results. Finally, we discussion and conclude our study in Section V.

II. Model Formulation

In our model, we classified the population into five compartments according to their states: the susceptible human (S), the exposed human (E), the infected human (I), the severe infected human (I_A) and the recovered human (R), We denote the total population by (N_T) .The dynamics transmission of disease associated with these compartments are illustrated as shown in Fig. 1.

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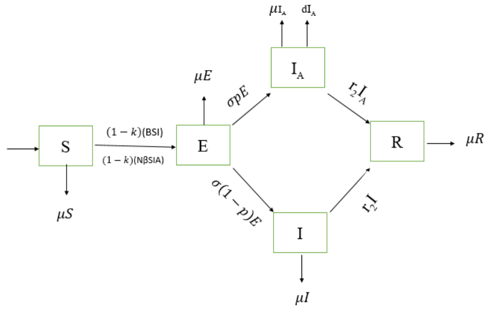


Fig. 1. Flow chart of the dynamical transmission of HFMD.

We defined,

S is the number of susceptible human population at time t

E is the number of exposed human population at time t

I is the number of infected human population at time t

I_A is the number of severe infected human population at time t

R is the number of recovered human population at time t

The transmission model will be a system of ordinary differential equations given by,

$$\frac{dS}{dt} = \Lambda-(1-k)\left(BSI + n\beta SI_A\right) - \mu S \tag{1}$$

$$\frac{dE}{dt} = (1-k)\left(BSI + n\beta SI_A\right) - \sigma(1-p)E - \sigma pE - \mu E \tag{2}$$

$$\frac{dI}{dt} = \sigma(1-p)E - r_2 I_A - \mu I \tag{3}$$

$$\frac{dI_A}{dt} = \sigma pE - r_1 I_A - \mu I_A - dI_A \tag{4}$$

$$\frac{dR}{dt} = r_2 I_A - r_2 I - \mu R \tag{5}$$

where

Λ is the birth rate of human population,

μ is the natural death rate of human population,

β is the probability of transmission,

n is the number of contacts,

$\frac{1}{\sigma}$ is the average of incubation period,

r_1 is the recovery rate of severe infected human,

r_2 is the recovery rate of infected human,

p is the fraction of developing infected cases,

d is the infected disease-related death rate,

k is the effectiveness of hand washing campaign,

with

$$N_T = S + E + I + I_A + R \tag{6}$$

By adding (1)-(5), we obtain

$$\frac{dN_T}{dt} = \Lambda - \mu N_T - \mu I_A \tag{7}$$

III. Model Analysis

A. Equilibrium Points

Disease free equilibrium point (E_0): there are no infected human and severe infected human, that is $I = 0,\ I_A = 0$. Substituting $I = 0,\ I_A = 0$ in (1)-(7), we obtained $E_0\left(S, E, I, I_A, N_T\right) = E_0\left(\frac{\Lambda}{\mu}, 0, 0, 0, \frac{\Lambda}{\mu}\right)$.

Endemic equilibrium point(E_1): In case $I^*>0,\ I_A^* > 0$.

We obtained,

$$E_1\left(S^*, E^*, I^*, I_A^*, N_T^*\right) =$$

$$\left(\frac{\Lambda}{(1-k)\left(\beta I^* + n\beta I_A^*\right)+\mu}, \frac{(1-k)\left(\beta I^* + n\beta I_A^*\right)\Lambda}{(\sigma+\mu)(1-k)\left(\beta I^* + n\beta I_A^*\right)+\mu}, I^*, I_A^*, \frac{\Lambda - dI_A^*}{\mu}\right)$$

where the value of I^* is a positive root of cubic equation,

$$H_1 I^{*3} + H_2 I^{*2} + H_3 I^* + H_4 = 0. \tag{8}$$

with

$$H_1 = A_2^{\ 2} A_6 - A_2 A_7 A_3,$$
$$H_2 = \left(A_1 A_7 - A_3 A_8\right) A_3 + A_2 A_4 A_7 - \left(A_1 A_6 - A_3 A_5 + A_1 A_6\right) A_2,$$
$$H_3 = A_4 A_8 A_3 - \left(A_1 A_7 - A_3 A_8\right) A_4 + \left(A_3 A_5 - A_1 A_6\right) A_1 + A_4 A_5 A_2,$$
$$H_4 = A_1 A_4 A_5 + A_4^2 A_8,$$
$$A_1 = \sigma\Lambda\beta(1-p)(1-k) - (r_2+\mu)\mu,\ A_2 = (r_2+\mu)(\sigma+\mu)(1-k)\beta,$$
$$A_3 = (r_2+\mu)(\sigma+\mu)(1-k)n\beta,\ A_4 = \sigma n\Lambda\beta(1-p)(1-k),$$
$$A_5 = \sigma p(1-k)n\Lambda\beta - \mu(r_1+\mu+d), A_6 = (r_1+\mu+d)(\sigma+\mu)(1-k)n\beta,$$
$$A_7 = (r_1+\mu+d)(\sigma+\mu)(1-k)\beta,\ A_8 = \sigma p(1-k)\Lambda\beta.$$

And the value of I_A^* is a positive root of cubic equation,

$$M_1 I_A^{*3} + M_2 I_A^{*2} + M_3 I_A^* + M_4 = 0 \tag{9}$$

where

$$M_1 = \left(A_2 A_6 - A_3 A_7\right) A_6,$$
$$M_2 = \left(A_3 A_5 - A_4 A_7\right) A_7 + \left(A_1 A_7 - 2A_2 A_5 + A_3 A_8\right) A_6,$$
$$M_3 = A_4 A_7 A_8 - A_1 A_6 A_8 - \left(A_1 A_7 - A_2 A_5\right) A_5 - \left(A_3 A_5 - A_4 A_7\right) A_8,$$
$$M_4 = A_1 A_5 A_8 - A_4 A_8^2.$$

Basic Reproductive number: We obtained a basic reproductive number $\left(R_0\right)$ by using the next generation matrix [7]. Rearrange the (1) - (4) and (7) in matrix form

$$F(x) = \begin{bmatrix} 0 \\ (1-k)\left(\beta SI + n\beta SI_A\right) \\ 0 \\ 0 \\ 0 \end{bmatrix}, V(x) = \begin{bmatrix} (1-k)\left(\beta SI + n\beta SI_A\right) + \mu S - \Lambda \\ \sigma(1-p)E + \sigma pE + \mu E \\ r_2 I + \mu I - \sigma(1-p)E \\ r_1 I_A + \mu I_A + dI_A - \sigma pE \\ \mu N_T + dI_A - \Lambda \end{bmatrix}$$

$$\frac{dx}{dt} = F(x) - V(x) \tag{10}$$

where $F(x)$ is the rate of appearance of new infections in compartment and $V(x)$ is the transfer of individuals out of compartment by all other means. Find the Jacobian of $F(x)$ and $V(x)$, denoted by $DF(x) = F$ and $DV(x) = V$, we obtained

$$F = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 \\ (1-k)\left(\beta I + n\beta I_A\right) & 0 & (1-k)\beta S & (1-k)n\beta S & 0 \\ 0 & \text{p} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

and

$$V=\begin{bmatrix} (1-k)(\beta I+n\beta I_A)+\mu & 0 & (1-k)\beta S & (1-k)n\beta S & 0\\ 0 & \sigma+\mu & 0 & 0 & 0\\ 0 & -\sigma(1-p) & r_2+\mu & 0 & 0\\ 0 & -\sigma p & 0 & r_1+\mu+d & 0\\ 0 & 0 & d & 0 & \mu \end{bmatrix}$$

Find F and V at $E_0(S,\ E,\ I,\ I_A,\ N_T)=E_0\left(\frac{\Lambda}{\mu},\ 0,\ 0,\ 0,\ \frac{\Lambda}{\mu}\right)$

We obtained,

$$F=\begin{bmatrix} 0 & 0 & 0 & 0 & 0\\ 0 & 0 & (1-k)\beta\frac{\Lambda}{\mu} & (1-k)n\beta\frac{\Lambda}{\mu} & 0\\ 0 & p & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$ and

$$V=\begin{bmatrix} \mu & 0 & (1-k)\beta\frac{\Lambda}{\mu} & (1-k)n\beta\frac{\Lambda}{\mu} & 0\\ 0 & \sigma+\mu & 0 & 0 & 0\\ 0 & -\sigma(1-p) & r_2+\mu & 0 & 0\\ 0 & -\sigma p & 0 & r_1+\mu+d & 0\\ 0 & 0 & d & 0 & \mu \end{bmatrix}$$

Find FV^{-1}, we get

$$FV^{-1}=\begin{bmatrix} 0 & 0 & 0 & 0 & 0\\ 0 & \frac{(1-p)(1-k)\sigma\beta\frac{\Lambda}{\mu}}{(\sigma+\mu)(r_2+\mu)}+\frac{(1-k)n\sigma p\beta\frac{\Lambda}{\mu}}{(\sigma+\mu)(r_1+\mu+d)} & \frac{(1-k)\beta\frac{\Lambda}{\mu}}{(r_2+\mu)} & \frac{(1-k)n\beta\frac{\Lambda}{\mu}}{(r_1+\mu+d)} & 0\\ 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

Find the spectral radius of FV^{-1} denoted by $\rho(FV^{-1})$

$$\rho(FV^{-1})=\begin{vmatrix} -\lambda & 0 & 0 & 0 & 0\\ 0 & \frac{(1-p)(1-k)\sigma\beta\frac{\Lambda}{\mu}}{(\sigma+\mu)(r_2+\mu)}+\frac{(1-k)n\sigma p\beta\frac{\Lambda}{\mu}}{(\sigma+\mu)(r_1+\mu+d)}-\lambda & \frac{(1-k)\beta\frac{\Lambda}{\mu}}{(r_2+\mu)} & \frac{(1-k)n\beta\frac{\Lambda}{\mu}}{(r_1+\mu+d)} & 0\\ 0 & 0 & -\lambda & 0 & 0\\ 0 & 0 & 0 & -\lambda & 0\\ 0 & 0 & 0 & 0 & -\lambda \end{vmatrix}$$

We obtain, the basic reproductive number as follow:

$$R_0=\sqrt{\frac{(1-p)(1-k)\sigma\beta\frac{\Lambda}{\mu}}{(\sigma+\mu)(r_2+\mu)}+\frac{(1-k)n\sigma p\beta\frac{\Lambda}{\mu}}{(\sigma+\mu)(r_1+\mu+d)}} \qquad (11)$$

Local Stability: The local stability of an equilibrium point is determined from the Jacobian matrix of the system of ordinary differential equation (1)-(4) and (6) evaluated at the equilibrium point. The Jacobian matrix at E_0 is

$$J_0=\begin{bmatrix} -\mu & 0 & -(1-k)\beta S & -(1-k)n\beta\frac{\grave{U}}{\mu} & 0\\ 0 & -\sigma-\mu & (1-k)\beta\frac{\grave{U}}{\mu} & (1-k)n\beta\frac{\grave{U}}{\mu} & 0\\ 0 & \sigma(1-p) & -r_2-\mu & 0 & 0\\ 0 & \sigma p & 0 & -r_1-\mu-d & 0\\ 0 & 0 & 0 & -d & -\mu \end{bmatrix}$$

The eigenvalues of the J_0 are obtained by solving equation $|J_0-\lambda I|=0$. We obtained the characteristic equation,

$$(\lambda+\mu)^2(\lambda^3+X_1\lambda^2+X_2\lambda+X_3)=0 \qquad (12)$$

where

$X_1=C_0+r_1+r_2+2\mu,\ C_0=\sigma+\mu$

$X_2=(r_1+\mu)(C_0+r_2+\mu)+(r_2+\mu)C_0-\sigma\beta\frac{\grave{U}}{\mu}(1-k)(np+1-p),$

$X_3=(r_1+\mu)(r_2+\mu)C_0-((r_2+\mu)np+(r_1+\mu+d)(1-p))(1-k)\sigma\beta\frac{\grave{U}}{\mu}.$

From the characteristic equation, We see that two are $\lambda_1=-\mu<0,\lambda_2=-\mu<0$. The other three eigenvalues are solution of $\lambda^3+X_1\lambda^2+X_2\lambda+X_3=0$. The roots of this equation will be negative if two coefficients satisfied with the Routh-Hurwitz criteria [8].

1) $X_1>0$, 2) $X_3>0$, 3) $X_1X_2>X_3$.

Endemic equilibrium point: To determine the stability of the endemic equilibrium point, E_1 by examining the eigenvalues of Jacobian matrix at E_1**,** which is

$$J_1=\begin{bmatrix} -(1-k)(\beta I^*+n\beta I_A^*)-\mu & 0 & -(1-k)\beta S^* & -(1-k)n\beta S^* & 0\\ (1-k)(\beta I^*+n\beta I_A^*) & -(\sigma+\mu) & (1-k)\beta S^* & (1-k)n\beta S^* & 0\\ 0 & \sigma(1-p) & -r_2-\mu & 0 & 0\\ 0 & \sigma p & 0 & -r_1-\mu-d & 0\\ 0 & 0 & 0 & -\mathrm{d} & -\mu \end{bmatrix}$$

and by solving equation $|J_1-\lambda I|=0$. We obtain the characteristic equation,

$$(\lambda+\mu)(\lambda^4+Q_1\lambda^3+Q_2\lambda^2+Q_3\lambda+Q_4)=0$$

where

$$Q_1=A+C+G+J,\ Q_2=K+(C+G+J)A$$
$$Q_3=AK+(H+F)BD-L,\ Q_4=(FJ+HG)BD-AL$$

$$A=(1-k)\left(\beta I^{*}+n\beta I_A^{*}\right)+\mu,\ B=(1-k)\left(\beta I^{*}+n\beta I_A^{*}\right),C=\sigma+\mu,$$
$$D=\sigma p,\ F=(1-k)\beta S^{*},G=r_2+\mu,\ J=r_1+\mu+d,\ H=(1-k)n\beta S^{*}$$
$$K=CG+(C+G)J-(H+F)D\ ,\ L=-CGJ+(FJ+GH)D\,.$$

We obtain the eigenvalues are $\lambda_1=-\mu<0$, and the remaining four eigenvalues of $\lambda^4+Q_1\lambda^3+Q_2\lambda^2+Q_3\lambda+Q_4=0$ will be negative real part if they satisfy the Routh - Hurwitz criteria [9] as follows.

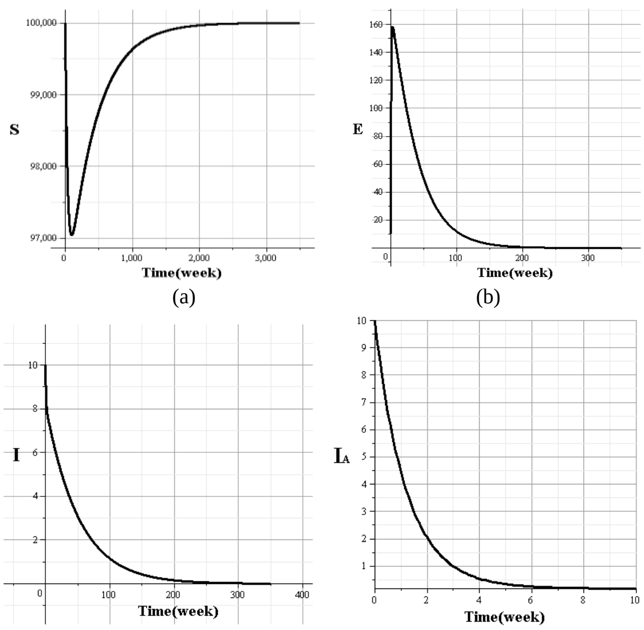
1) $Q_1>0$, 2) $Q_1Q_2-Q_3>0$, 3) $Q_1(Q_2Q_3+Q_1Q_4)-Q_3^2>0$,
4) $Q_4(-Q_3^2+Q_1Q_2Q_3-Q_1^2Q_4)>0$.

IV. Numerical Results

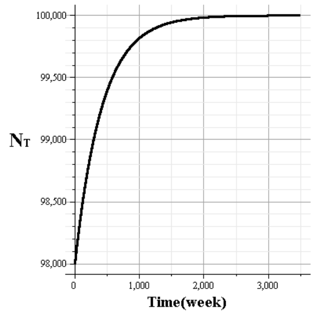
In this study, we are interested in the transmission model of HFMD with the effectiveness of hand washing campaign. The system is simulated for various set of parameters. The stability of disease free equilibrium point (E_0) and endemic equilibrium point (E_1) are shown in Fig. 2 and Fig. 3, respectively. The values of parameters used for simulation in this model as shown in Table I.

TABLE I: Parameter Values Used in Numerical Simulation

Parameters	Description	Values
Λ	Birth rate of human population	100000/(420) per week
μ	Natural death rate of human population	1/(420) per week
β	Probability of transmission	0.00007
n	Number of contacts	0.00001 per week
σ	Average of infectious period	4/7 per week
r_1	Recovery rate of severe infected human	0.8235 per week
r_2	Recovery rate of infected human	0.8235 per week
p	Fraction of developing infected cases	0.025 per week
d	Death rate related infected disease	0.01 per week
k	Effectiveness of hand washing campaign	0.90



(a) (b)
(b) (d)



(e)

Fig. 2. Time series of (a) Susceptible human (S), (b) Exposed human (E), (c) Infected human (I), (d) Severe Infected human (I_A), and (e) Total human (N_T) proportion approach to the disease free equilibrium state E_0.

Stability of disease free state: From the values of parameters listed in Table I, we obtain the values of eigenvalues and basic reproductive number is:

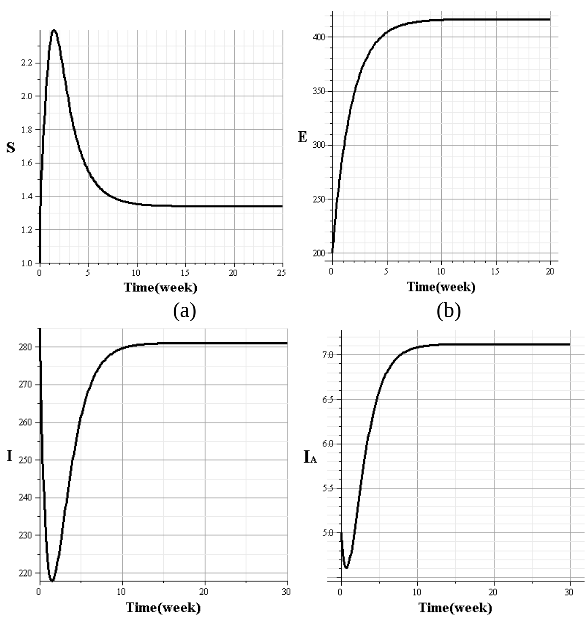
$$\lambda_{1,2}=-0.00238095, \lambda_3=-1.33085, \lambda_4=-0.835949,$$
$$\lambda_5=-0.0587765,\ R_0=0.8229.$$

Since all of these eigenvalues are to be negative and the basic reproductive number is less than one ,the equilibrium state will be disease free state, $E_0(100{,}000,\ 0,\ 0,\ 0,\ 100{,}000)$ as shown in Fig. 2.

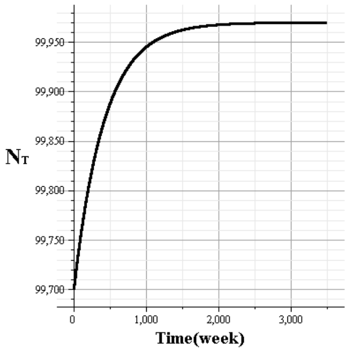
Stability of endemic state: We change the values of effectiveness of hand washing campaign to be $k=0.10$ and $\beta=0.70$, $n=0.10$. The other values of parameters are listed in Table I. We obtain the values of eigenvalues and basic reproductive number is:

$$\lambda_1=-0.00238095, \lambda_2=-177.501, \lambda_3=-1.74063,$$
$$\lambda_{4,5}=-0.244385\pm0.521022i, R_0=2.7215.$$

Since all of these eigenvalues are to be negative and the basic reproductive number is greater than one ,the equilibrium state will be disease free state, $E_1(1.3414,\ 414.9322,\ 281.0242,\ 7.0913,\ 99970.2162)$ as shown in Fig. 3.



(a) (b)
(c) (d)



(e)

Fig. 3. Time series of (a) Susceptible human (S), (b) Exposed human (E), (c) Infected human (I), (d) Severe Infected human (I_A), and (e) Total human (N_T) proportion approach to the endemic equilibrium state E_1.

V. Conclusion

We formulate the transmission model of HFMD by incorporating the effect of hand washing campaign to protect individual from HFMD. The basic reproductive number is $\mathcal{R}_0=\sqrt{R_0}$,where

$$R_0=\frac{(1-p)(1-k)\sigma\beta\frac{\Lambda}{\mu}}{(\sigma+\mu)(r_2+\mu)}+\frac{(1-k)n\sigma p\beta\frac{\Lambda}{\mu}}{(\sigma+\mu)(r_1+\mu+d)}$$

Hence, R_0 represent the average number of secondary infections produce when one infected individual is introduced into a host population where everyone is susceptible [10]. In addition, R_0 is the threshold condition for determining the stability of the system. If $R_0<1$, the disease free equilibrium point is local asymptotically stable as shown in Fig. 2, that is disease will die out from the community. If $R_0>1$, the endemic equilibrium point is local asymptotically stable as shown in Fig. 3, that is the disease will persist in the community. For the endemic state the value is greater than one due to young children do not know how to protect themselves from the infected children [1].

We can conclusion that if each individual who live in the community has knowledge, attitude and behavior to protect them from HFMD by increasing the effectiveness of hand washing campaign. The number of susceptible human to contact the HFMD will decrease. In young children school or nursery and kindergarten, as HFMD has occurred. This alternative intervention could decrease the number of infected human by hand washing campaign for all young students at schooldays.

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