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Pneumonia Control Measures Under Five Year Children

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Abstract: *Pneumonia is one of the leading causes of serious illness and deaths among children around the world. In this paper we develop a deterministic Susceptible-Exposed-Infectious-Recovered or SEIR model to study the spread of pneumonia using data from the Boloso Sore of Ethiopia. The study also evaluates the impact of control measures, mainly vaccination, the spread Streptococcus pneumonia disease. Conditions for the clearance or persistence of the pneumonia infection through the stability of the equilibria are derived. The vaccine impact to assess the degree of transmission as well as to determine the power of the vaccine in reducing the transmission is calculated. It is concluded that rapid vaccination is the most important factor to control the spread of streptococcus pneumonia in the case of an outbreak and that of the susceptible population needs to be vaccination in order to bring the disease under control. Numerical simulation study in made and it is observed that a combination of vaccination programs targeting children can effectively eliminate the pneumonia infection from the population.*

Key words: *Pneumonia, Mathematical modeling, SEIR Modeling, vaccination, stability, basic reproduction number.*

I. Introduction

Pneumonia is an air-borne respiratory disease caused by infection inside the lungs. It may be contacted by breathing in droplets containing disease causing organisms, released into air when an infected person coughs or sneezes .Pneumonia may also be contacted when bacteria or viruses that are normally present in the mouth, throat, or nose inadvertently enter the lungs. The most common cause of bacterial pneumonia is Streptococcus pneumonia. The symptoms of pneumonia include: cough, difficult breathing, fever, muscle aches, loss of appetite and lethargy. The risk factors for pneumonia include smoking and passive smoking, alcohol and drug abuse, crowded living conditions and certain medical conditions. These include conditions that interfere with the gag relax; weaken the immune system and organ transplant. A weak immune system may be as a result of prolonged malaria exposure, malnutrition among other factors. Children have a higher risk of developing pneumonia if they have weakened immune systems [15].

Vaccines to prevent certain types of pneumonia are available. Treatment depends on the underlying cause. Pneumonia presumed to be bacterial is treated with antibiotics. If the pneumonia is severe, the affected person is generally hospitalized [5]. Current Streptococcus pneumonia vaccines are based on the use of the bacterial capsular polysaccharides (PS), which induce specific type antibodies that activate and fix complement and promote bacterial opsonization and phagocytosis. The two types of currently licensed vaccines are the pneumococcal polysaccharide vaccine (PPV), based on purified capsular (PS) and pneumococcal conjugate vaccines (PCV), and obtained by chemical conjugation of the capsular (PS) to a protein carrier [1].

Some of these vaccines have a proven record of safety e.g. PPV in pregnant and breast-feeding mothers for preventing pneumococcal pneumonia in young infants [13]. Statistics shows that of all children outpatients suffering from respiratory complications, every year 1.9 million children under 5 years of age die from Pneumonia [11]. Looking at the situations, pneumonia is the single leading cause of death among children younger than five years in Ethiopia. The 2008 WHO report showed there were 389,000 under five deaths, of which 22 percent were due to pneumonia1. In 2010, pneumonia was responsible for 21 percent of all under five deaths in the country, only one percent reduction over the 4 years period.

According to the recent 2014 countdown to 2015 report, however, the toll of in 5 deaths of pneumonia has supposedly to 18 percent, which is among the highest even compared to the load in the majority of African countries. Nonetheless, there are only scant source of data on this problem locally. For instance, a case control study in Gilgel Gibe revealed that 42 percent of post neonatal and 22:6 percent of neonatal mortality were attributable to pneumonia. (Ethiopia. J. Health Dev. 2014/15).

Therefore to realize the Millennium Development Goal 4 or MDG 4, in this study, we develop and analyze using mathematical models the pneumonia dynamics under five years children in particular Boloso Sore Woreda, Wolaita Zone, SNNPR, Ethiopia. For this study we use the secondary data of 2014-15. An SEIR model is formulated and is used to find local and global stability of disease free equilibrium point or DFE and local stability of an endemic equilibrium point or EEP. The model will be simulated to determine the behavior of each embedded parameter for the impact of control measures of pneumonia. Numerical study and validation of the

model, estimated and secondary data is used. Simulation of the model is also done with MATLAB by using ode45 method.

II. Model formulation

The model we formulate here is an SEIRS model, where the population is divided into compartments containing susceptible, exposed, infectious and recovered individuals. Compartments with labels S, E, I, R are used for epidemiological classes as shown in Figure 1. The class S is the class of susceptible individuals; that is, those who can become infected. When there is an adequate contact of a susceptible with an infective so that transmission occurs, the susceptible enters the exposed class E of those in the latent period, who are infected but not yet infectious. At the end of the latent period, the individual enters the class I of infective, who are capable of transmitting the infection (that is, infectious). At the end of the infectious period, the individual enters the recovered class R. At time t, there are S(t) susceptible, E(t) exposed, I(t) infectious and R(t) recovered individuals in the population of constant size, N. The model assumes that all new-born are susceptible i.e., no vertical transmission to the infection and are recruited at rate µN. The susceptible are exposed to the infection once in contact with an infectious individual. The exposed become infected at rate αE and the infectious individuals recover from the infection at rate γI. The transmission coefficient β , the latency coefficient α , the recovery coefficient γ and the capital death rate μ are positive quantities. Figure 1 represents the epidemiological model between classes of susceptible, exposed, infectious and recovered individuals in the population and $N = S(t) + E(t) + I(t) + R(t)$.

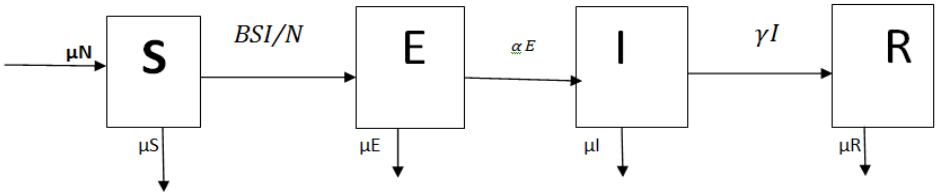

Figure 1: Schematic Diagram for SEIRS Model without vaccination

The following system of ordinary differential equations, ODEs, is formulated to represent the model

$dS/dt = \mu N - \mu S - (\beta SI/N)$ (1)
$dE/dt = (\beta SI/N) - (\mu + \alpha)E$ (2)
$dI/dt = \alpha E - (\mu + \gamma)I$ (3)
$dR/dt = \gamma I - \mu R$ (4)

The nonlinear system of differential equations formulated above has initial conditions which are $S(t_0) = S_0, E(t_0) = E_0, I(t_0) = I_0, R(t_0) = R_0$ all positive quantities. Expressing equation (1-4) as a proportion of the population we obtain

$u(t) = S(t)/N, v(t) = E(t)/N, w(t) = I(t)/N, z(t) = R(t)/N$ (5)

Here $Z(t) = 1 - u(t) - v(t) - w(t)$. Now, on substituting equation (5) into equation (1-4) we obtain

$du/dt = \mu - u(\mu + \beta w)$ (6)
$dv/dt = \beta wu - (\mu + \alpha)v$ (7)
$dw/dt = \alpha v - (\mu + \gamma)w$ (8)
$dz/dt = \gamma w - \mu z$ (9)

Hence, we have equations (6-9) which reduces to three dimensional system of (1-4). Now the basic reproductive ratio (R_0) will be found by using the method of general matrix

$R_0 = \beta\alpha / (\mu + \alpha)(\mu + \gamma)$ (10)

The stability of the model is obtained by evaluating at steady state of the system of the equations (6-8). We consider two states the infectious free state for which $w = 0$ and endemic state for which $w \neq 0$.

That is

$\mu - u(\mu + \beta w) = 0$ (11)
$\beta wu - (\mu + \alpha)v = 0$ (12)
$\alpha v - (\mu + \gamma)w = 0$ (13)

Solving the equations (11-13) at $w = 0$, we get $u = 1, v = 0$, the first equilibrium point is $(u, v, w) = (1, 0, 0)$ and is disease free equilibrium point. In case of endemic state $(w \neq 0)$, we set $v = [\gamma + (\mu/\alpha)]$w using the equation (13) substituting the value of v into equation (12) to obtain $u = [(\mu + \alpha)(\mu + \gamma)/\beta\alpha] = 1/R_0$. Using the value of u in equation (11) we obtain $v = \{[\mu(R_0 - 1)]/[R_0(\mu + \alpha)]\}$ and $w = [\mu(R0 - 1)]/\beta$.

Hence, endemic equilibrium state takes the form $(u, v, w) = (1/R_0,\ \mu(R_0 - 1)/R_0(\mu + \alpha),\ \ \mu(R_0 - 1)/\beta)$. We evaluate the local stability of the steady state by linearization the equations (6-8). The Jacobian matrix found to be

$$J = \begin{pmatrix} -\mu - \beta w & 0 & -\beta u \\ \beta w & -(\mu + \alpha) & \beta u \\ 0 & \alpha & -(\mu + \gamma) \end{pmatrix} \quad (14)$$

We evaluate the Jacobian matrix at the disease free equilibrium $(u, v, w) = (1,0,0)$ to obtain

$$J_{DEF} = \begin{pmatrix} -\mu & 0 & -\beta \\ 0 & -(\mu + \alpha) & \beta \\ 0 & \alpha & -(\mu + \gamma) \end{pmatrix}$$

To determine eigenvalues for DFE we consider Jacobian matrix of the model equation (14)

$$J_{DEF} - \lambda \mathrm{I} = \begin{pmatrix} -\mu - \lambda & 0 & -\beta \\ 0 & -(\mu + \alpha) - \lambda & \beta \\ 0 & \alpha & -(\mu + \gamma) - \lambda \end{pmatrix} \quad (15)$$

This gives the characteristic equation $\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$

where $a_1 = 3\mu + \alpha + \gamma$, $a_2 = (\mu + \alpha)(\mu + \gamma) - \alpha\beta + \mu(2\mu + \alpha + \gamma)$, and $a_3 = \mu((\mu + \alpha)(\mu + \gamma) - \alpha\beta)$. From Routh – Hurwitz stability criterion if the conditions $a_1 > 0$, $a_3 > 0$ and $(a_1 a_2 - a_3) > 0$ (Flores, 2013) are true. If $a_3 < 0$ then the free equilibrium point is in an unstable steady state. This means the presence of a person infected with pneumonia in a completely susceptible population will eventually result in an outbreak of the disease.

$$J_{EE} - \mathrm{wI} = \begin{pmatrix} -\mu R_0 - w & 0 & -(\mu + \alpha)(\mu + \gamma)/\beta \\ -\mu(R_0 - 1) & -(\mu + \alpha) - w & (\mu + \alpha)(\mu + \gamma)/\beta \\ 0 & \alpha & -(\mu + \gamma) - w \end{pmatrix} \quad (16)$$

This gives the characteristic equation $w^3 + b_1 w^2 + b_2 w + b_3 = 0$ where $b_1 = \mu R_0 + 2\mu + \alpha + \gamma$, $b_2 = (2\mu + \gamma + \alpha)\mu R_0$ and $b_3 = \mu(R_0 - 1)(\mu + \alpha)(\mu + \gamma)$. In the endemic equilibrium EE state $(u, v, w) = (1/R_0,\ \mu(R_0 - 1)/R_0(\mu + \alpha),\ \mu(R_0 - 1)/\beta)$. Routh – Hurwitz stability criteria is satisfied. Hence the endemic steady state is stable. This means the pneumonia disease would spread.

III. Modeling Pneumonia with inclusion of control strategy

We extend the SEIR model to take care of effect of vaccination on the spread of pneumonia, the class S of susceptible is increased by birth and natural death at a rate μ.The class E of exposed individuals is generated through contact with infected individuals at rate β. The class S is decreased by testing and pneumonia therapy at a rate δ , breaks through into expose class at a rate α and diminished by natural death at a rate μ. The class I of infected individuals is generated by breakthrough of exposed individuals at a rate α. The class is decreased by recovery from infection at a rate γ and diminished by natural death at a rate μ. The model assumes that both recovered susceptible individuals and recovered infected individuals become permanently immune to the disease. This generates a class R of individuals who have complete protection against the disease. The R of recovered individuals diminished by natural death at a rate of μ.

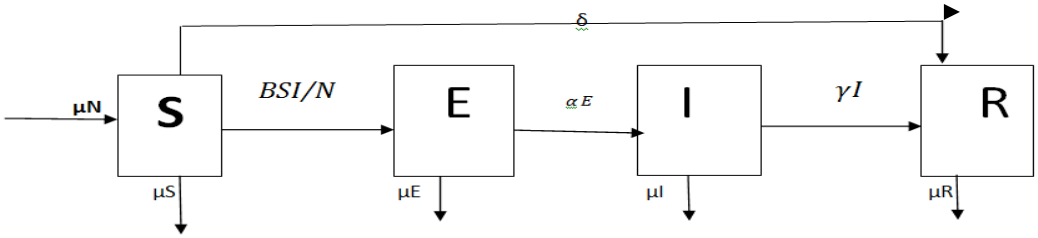

Figure 2: Schematic diagram for Vaccination *SEIR* model

The transition between model classes can now be expressed by the following system of differential equations:

$dS/dt = \mu N - (\beta SI/N) - \mu S - \delta S$ (17)
$dE/dt = (\beta SI/N) - (\mu + \alpha)E$ (18)
$dI/dt = \alpha E - (\mu + \gamma)I$ (19)
$dR/dt = \gamma I + \delta S - \mu R$ (20)

We now find equilibrium point (u, v, w, z) from equations (17) to (20) as a proportion of the population $u(t) = [S(t)/N]$, $v(t) = [E(t)/N]$, $w(t) = [I(t)/N]$, and $z(t) = [R(t)/N]$. Thus, $u(t) + v(t) + w(t) + z(t) = 1$ and we obtain the following.

$du/dt = \mu - u(\mu + \beta w + \delta)$ (21)
$dv/dt = \beta wu - (\mu + \alpha)v$ (22)
$dw/dt = \alpha v - (\mu + \gamma)w$ (23)
$dz/dt = \gamma w + \delta u - \mu z$ (24)

For stability of the model we need to evaluate the steady state of the system of the equations from (21) to (24), which leads to

$\mu - u(\mu + \beta w + \delta) = 0$ (25a)
$\beta wu - (\mu + \alpha+)v = 0$ (25b)
$\alpha v - (\mu + \gamma)w = 0$ (25c)
$\gamma w + \delta u - \mu z = 0$ (25d)

Now, the basic reproduction number R_0 will be found by using the method of next generation matrix and can be described as $R_0 = \rho(FV^{-1})$ where $F = \begin{pmatrix} 0 & \beta \\ 0 & 0 \end{pmatrix}$ and $V = \begin{bmatrix} 1/(\mu+\alpha) & 0 \\ -\alpha & (\mu+\gamma) \end{bmatrix}$. Hence, the reproductive number will have the expression as $R_0 = \{\beta\alpha/[(\mu + \alpha)(\mu + \gamma)]\}$. We consider two states, infection-free state where $w = 0$ and endemic state where $w \neq 0$. Equations (25) have a disease free equilibrium. At the infection-free state when $w = 0$, the values take the form $u = [\mu/(\mu + \delta)]$, $v = 0$ and $z = [\delta/(\mu + \delta)]$. We now evaluate Jacobian matrix below:

$$J(u, v, w, z) = \begin{bmatrix} -\mu - \beta w - \delta & 0 & -\beta u & 0 \\ \beta w & -(\mu + \alpha) & \beta u & 0 \\ 0 & \alpha & -(\mu + \gamma) & 0 \\ \delta & 0 & \gamma & -\mu \end{bmatrix} \quad (26)$$

At the equilibrium point $(u, v, w, z) = (u, 0, 0, z)$ the matrix (26) takes the form as

$$J(u, 0, 0, z) = \begin{bmatrix} -\mu - \delta & 0 & -\beta u & 0 \\ 0 & -(\mu + \alpha) & \beta u & 0 \\ 0 & \alpha & -(\mu + \gamma) & 0 \\ \delta & 0 & \gamma & -\mu \end{bmatrix} \quad (27)$$

At the endemic equilibrium point $w \neq 0$ we have $u = (1/\mathrm{R}_0)$, $V = \{\mu/\{(\mu + \alpha)[1 - (\rho/R_0)]\}\}$, $w = \{\mu\alpha/\{(\mu + \gamma)(\mu + \alpha)[1 - (\rho/R_0)]\}\}$ and $z = \{\{\gamma\alpha/(\mu + \alpha)(\mu + \gamma)[1 - (\rho/R_0)]\} - (\delta/\mu R_0)\}$ and the Jacobian matrix reduces to

$$J_{EE} = \begin{pmatrix} -\mu - \beta w - \delta & 0 & \beta u & 0 \\ \beta w & -\mu - \alpha & \beta u & 0 \\ 0 & \alpha & -\mu - \gamma & 0 \\ 0 & 0 & \gamma & -\mu \end{pmatrix} \quad (28)$$

The disease free – equilibrium point is given by $(u, v, w, z) = (u, 0, 0, z)$. We evaluate the Jacobian matrix and find the eigenvalues at this equilibrium point. Thus, we construct the determinant equation as

$$|J_{DFE} - \lambda I| = \begin{vmatrix} -\mu - \delta - \lambda & 0 & -\beta u & 0 \\ 0 & -(\mu + \alpha) - \lambda & \beta u & 0 \\ 0 & \alpha & -(\mu + \gamma) - \lambda & 0 \\ \delta & \delta & \gamma & -\mu - \lambda \end{vmatrix} = 0 \quad (29)$$

The evaluation of the determinant (29) gives the characteristic equation in its simplified form as $(\mu + \delta + \lambda\mu + \lambda\lambda^2 + \mu + \alpha\mu + \gamma\lambda + 2\mu + \alpha + \gamma - \mu + \alpha\mu + \gamma = 0$. The eigenvalues of J_{DFE} matrix are $\lambda_1 = -\mu - \delta$, $\lambda_2 = -\mu$, $\lambda_3 = -(\mu + \alpha)$, and $\lambda_4 = -\{[\beta\alpha\mu/(\mu + \delta)] + (\mu + \gamma)\}$. Since these four eigenvalues are all negatives the disease free equilibrium point is stable.

Further, the endemic equilibrium point where $w \neq 0$, we have $u = (1/R_0)$, $v = \{\mu/\{(\mu + \alpha)[1 - (\rho/R_0)]\}\}$, $w = \{\mu\alpha/\{(\mu + \gamma)(\mu + \alpha)[1 - (\rho/R_0)]\}\}$ and $z = \{\{\gamma\alpha/(\mu + \alpha)(\mu + \gamma)[1 - (\rho/R_0)]\} -$

$(\delta/\mu R_0)\}$. We evaluate the Jacobian matrix and find the eigenvalues at this endemic equilibrium point. Thus, we construct the determinant equation as

$$\left|J_{EE} - Y\,I\right| = \begin{vmatrix} -\mu R_0 - \delta - Y & 0 & -(\beta / R_0) & 0 \\ \mu(R_0 - \rho) & -(\mu+\alpha) - Y & (\beta/R_0) & 0 \\ 0 & \alpha & -(\mu+\gamma) - Y & 0 \\ \delta & 0 & \gamma & -\mu - Y \end{vmatrix} = 0 \quad (30)$$

The evaluation of the determinant (30) gives the characteristic equation in its simplified form as $(Y + \mu\ Y^3 + x_1 Y^2 + x_2 Y + x_3 = 0$ where $x_1 = \mu\ (R_0 + \rho + 1) + \delta + 2\mu + \alpha + \gamma$, $x_2 = \mu\ R_0 + \rho + 1 + \delta\ 2\mu + \alpha + \gamma + \mu + \alpha\ \mu + \alpha$ and $x_3 = \mu\ [(R_0 + \rho + 1) + \delta]\ (\mu + \gamma)\ (\mu + \alpha) + \mu\ [(\mu + \gamma)\ (\mu + \alpha)\ \rho - \alpha\beta)]$. From Routh – Hurwitz stability criterion if the conditions $a_1 > 0$, $a_3 > 0$ and $(a_1 a_2 - a_3) > 0$ (Flores, 2013) are true, then all the roots of the characteristic equation have negative real part which means that it is a stable equilibrium point.

IV. Model Application

In this section, we study $SEIR$ model using data from the Boloso Sore Woreda, Ethiopia. Analysis of the data indicates that during July 2014 – June 2015 a total of 846 people attended hospitals for flu screening and 477 people were found to be infected by pneumonia. The data are $(S,\ E,\ I,\ R) = (27391,\ 4388,\ 477,\ 466$ by dividing through by the total population of Boloso Sore Ethiopia which is $N = 32{,}722$, we have $u = 0.0.8370,\ v = 0.1341,\ w = 0.00145$ and $z = 0.0145$ as initial proportion of susceptible, exposed, infectious and recovered respectively.

The basic reproductive is found be to $R = 4.6136$. The free equilibrium $(u\,.v, w) = (1, 0, 0)$ is unstable and endemic for equilibrium $(u,\ v,\ w) = (0.8370,\ 0.1341,\ 0.0145)$ is stable. In $SEIR$ model vaccination both with free and endemic equilibriums are stable. The solutions to the pneumonia model equations are obtained with the Matlab $ODE45$ solver Runge Kutta method. We also determine the stability of the equilibrium points of the $SEIR$ model and perform sensitivity analysis on the parameter values to determine the effect on the spread of pneumonia in Ethiopia.

V. Numerical simulation

5.1 Disease free equilibrium and endemic equilibrium

This part gives an illustration of the analytical results of the model by carrying out stability analysis and numerical simulations of the model using the parameter values pertinent to Ethiopia in Boloso Sore in 2014 – 15 .If the value of the parameters are $\mu = 0.0012,\ \gamma = 0.1176,\ \alpha = 0.5,\ \beta = 0.5445$, then the effects on the reproduction number $R_0 = 4.5724$ and the stability of the disease – free equilibrium and endemic equilibrium points are shown graphically below:

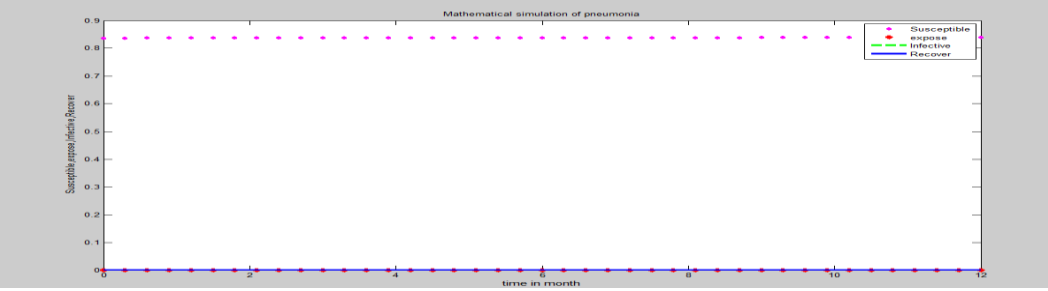

Figure 3: Simulation of the SEIR model without vaccination of pneumonia at free-equilibrium point

We find that, the initial proportion of infectious has small or no effect on the susceptible population and hence we have disease – free equilibrium state.

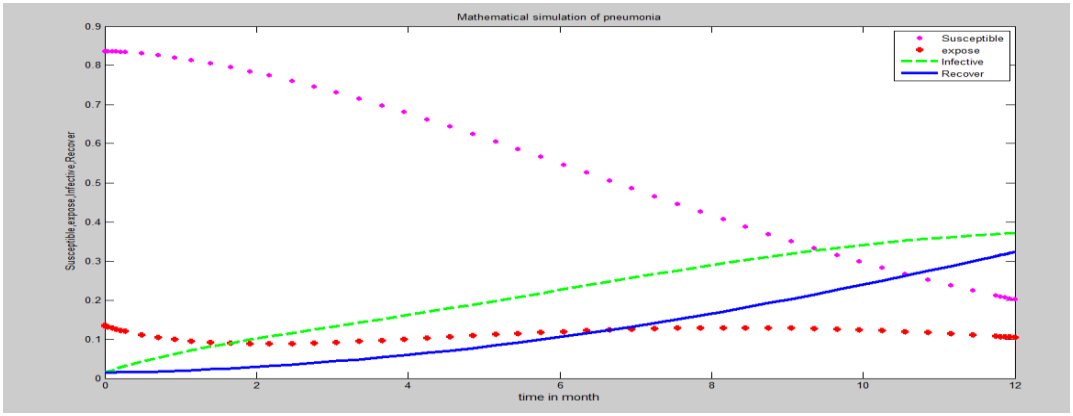

Figure 4: Simulation of SEIR model without vaccination of pneumonia at Endemic equilibrium point

Fig 4 showing results that the endemic equilibrium state of SEIR model exhibit susceptible individual decrease with increase in time. The exposed individual at latent period decreases slightly and then increases hence as more and more people are infected with the pneumonia, the disease become endemic in the country.

5.2 Numerical simulation of SEIR model with vaccination

5.2.1 Disease free equilibrium and endemic equilibrium point

If the value of the parameter are $\mu = 0.0012$, $\gamma = 0.1176$, $\alpha = 0.5$, $\beta = 0.5445$ and $\delta = 0.966$ the effects on the reproduction number $R_0 = 1.6447$ and the stability of the disease free equilibrium and endemic equilibrium as shown in figures 5 and 6.

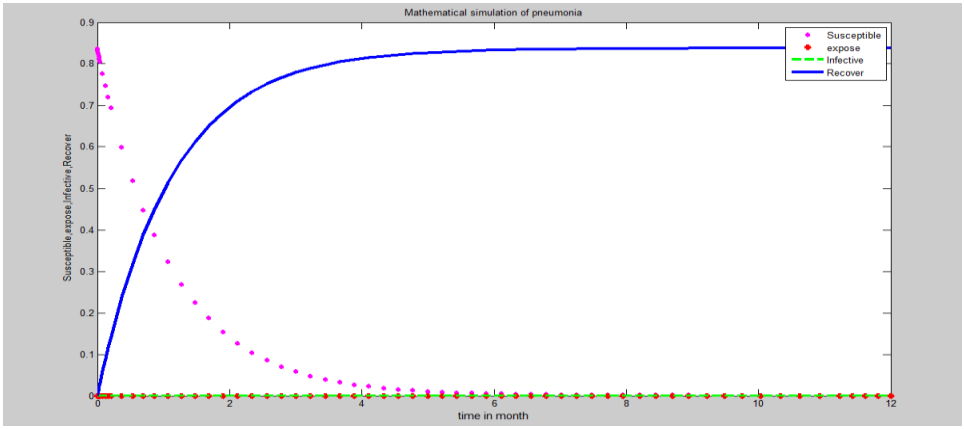

Figure 5: Simulation of the SEIR model with vaccination pneumonia at Free – Equilibrium Point

From fig .5 we see that the susceptible population decreases as time increases. This decrease may be possibly because of the high rate of recovery due to mass vaccination, as individuals become permanently immune upon recovery free equilibrium state.

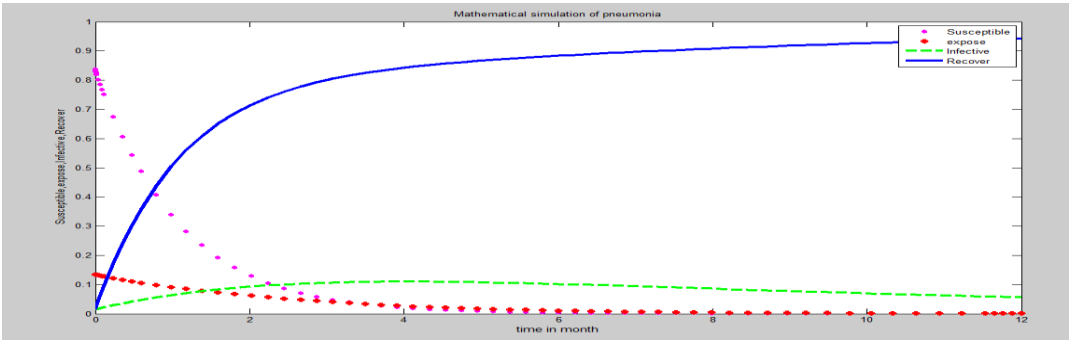

Figure 6: Simulation of the SEIR model with vaccination pneumonia at endemic point

From fig 6, we see that the susceptible population decreases as time increases. This decrease may be possibly because of the high rate of recovery due to mass vaccination, as individuals become permanently immune upon recovery. Exposed individuals show some rapid decrease after the earlier intervals of rise, the decrease in the exposed population could be due to early detection and also possibly due to those who enter the infective class. Infected individuals at the very beginning rise sharply as the rate increases and then fall uniformly as time increases. This rapid decline of the infected individuals may be due to early detection of the pneumonia and partly due to those who revert to the Exposed class. It can also be observed that the population of the recovered individuals rise up steadily for some number of months and then drops and remains nearly a constant. This could be due to the greater number of infectious individuals who have been treated for the Pneumonia transmission

VI. Conclusions

The present model has shown success in attempting to predict the causes of pneumonia transmission within the Boloso sore Ethiopia. The model strongly indicates that the spread of the disease largely depends on the contact rates with infected individuals within children. From the results, it is seen that the reproduction number without vaccination for SEIR epidemiological model indicates that $R_0 > 1$. The sensitivity analysis reveals that whenever the infectious rate is increased or the recovery rate is increased, the disease would spread. But with vaccination the disease infectious rate is reduced or the recovery rate is increased. This means that as more and more children are infected with the pneumonia without vaccination, since vaccination intervention has significant impact on the reduction of the disease, if it is implemented at targeted scale in endemic disease community, then new generation free of pneumonia disease in terms of different transmission level can be expected.

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