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Vaccinated Susceptible Infected and Recovered (VSIR) Mathematical Model to Study the Effect of Bacillus Calmette-Guerin (BCG) Vaccine and the Disease Stability Analysis

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Abstract**—**Tuberculosis (TB) remains a leading cause of infectious mortality. It is primarily transmitted by the respiratory route, individuals with active disease may infect others through airborne particles which releases when they cough, talk, or sing and subsequently inhale by others. In order to study the effect of the Bacilli Calmette-Guerin (BCG) vaccine after vaccination of TB patient, a Vaccinated Susceptible Infected and Recovered (VSIR) mathematical model is being developed to achieve the desired objectives. The mathematical model, so developed, shall be used to quantify the effect of BCG Vaccine to protect the immigrant young adult person. Moreover, equations are to be established for the disease endemic and free equilibrium states and subsequently utilized in disease stability analysis. The stability analysis will give a complete picture of disease annihilation from the total population if the total removal rate from the infectious group should be greater than total number of dormant infections produced throughout infectious period.

Keyword**—**Bacillus Calmette-Guerin vaccine, disease-free equilibrium state, VSIR Quantification, disease stability analysis.

I. Introduction

TUBERCULOSIS (TB) is a contagious bacterial infection caused by Mycobacterium Tuberculosis. It usually affects the vital organs such as lungs, central nervous system, lymphatic system, brain, spine and kidneys. Only people who have pulmonary TB are infectious [1]. TB spreads from person to person through coughs, sneezes, speaks, spits, and kisses. Mycobacterium Tuberculosis can be easily infected and more likely to develop the active TB in the individual. After a person becomes infected, the tuberculosis bacteria are controlled by the person's immune system. When the bacteria spread out of control, the infection becomes active, and a person can have active or latent TB. Both active and latent TB is treatable and curable. However in order to prevent the individual, there is an earnest need to strengthen the body immune system and timely vaccination within the desired period. BCG vaccine plays an important role in this menace [2]. The disease is responsible for approximately two million deaths each year. Although TB is currently well-controlled in most countries, recent data indicates that the overall global incidence of TB is rising as a result of resurgence of disease in Africa and parts of Eastern Europe and Asia [3].

Mathematical models developed played a key role in the formulation of TB control strategies. Most of these models are of the VSIR class in which the collection population is categorized by infection as Vaccinated, Susceptible, Infected and Recovered. One-third of the world's population is currently infected with the TB bacillus and new infections are occurring in the individual at a rate of one per second [1].

Bacillus Calmette-Guerin or Bacilli Calmette-Guerin (BCG) is a vaccine against tuberculosis that is prepared from a strain of the attenuated (destabilized) live bovine tuberculosis bacillus, Mycobacterium bovine that has lost its virulence in humans by being specially cultured in an artificial medium for years. The bacilli have retained enough strong antigen cities to become human tuberculosis. At best, the BCG vaccine is 80% somewhat effective vaccine for the prevention of effective in preventing tuberculosis for duration of 15 years. However its protective effect appears to vary according to geography [4]. There are three main factors that determine the risk of becoming exposed to tubercle bacilli; they include, the number of incident infectious cases in the community, the duration of infectiousness and the number and nature of interactions between a case and a susceptible contact per unit of time of infectiousness [5]. It may be mentioned here that not everyone infected with Mycobacterium Tuberculosis becomes sick, after a person becomes infected. The tuberculosis bacteria are controlled by the person's immune system. When the bacteria spread out of control, the infection becomes active. A person can have active or latent (motionless) TB. Both active and latent TB is treatable and curable. Active TB means the bacteria are active in the body and they weaken the immune system. Only people with active TB can spread the disease. People with latent TB does not feel sick and do not have any symptoms. According to the World Health Organization (WHO), young person infected with Mycobacterium Tuberculosis are also more likely to develop active TB than older people since their immune system are not yet well developed [6].

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Mathematical model developed for the tuberculosis disease population dynamics and posits that population dynamics depends more on the number of actively infected people in the population at the initial time and also on the disease incidence transmission rate at a given time. Also, it was shown that the disease free equilibrium is stable while the endemic equilibrium may or may not be stable on the various values of the model parameter [7].

In this research, the effect of BCG vaccine is used as in preventing and control of tuberculosis among young persons. Besides, the disease equilibrium state and the stability analysis have also been carried out with the help of constructed model. Lastly, outcomes have been presented with comprehensive argument to accomplish the model authentications.

II. Methods

In an Analytic method we consider a two-dimensional discrete-time system:

$$x_{n+1} = f(x_n, y_n)$$
$$y_{n+1} = g(x_n, y_n)$$

The qualitative analysis of a higher dimensional discrete time system is complicated, and similar to a two –dimensional discrete-time system

The logic as in the scalar case, equilibrium (x^*, y^*) satisfy

$$x^* = f(x^*, y^*)$$
$$y^* = g(x^*, y^*)$$

Stability of equilibrium (x^*, y^*) can be determined by the following theorem [8].

Theorem: Linear stability analysis

Let (x^*, y^*) be equilibrium of

$$x_{n+1} = f(x_n, y_n)$$
$$y_{n+1} = g(x_n, y_n)$$

and f, g are at least twice continuously differentiable. Let

$$J(x^*, y^*) = \begin{pmatrix} \frac{\partial f}{\partial x_n}(x^*, y^*) & \frac{\partial f}{\partial y_n}(x^*, y^*) \\ \frac{\partial g}{\partial x_n}(x^*, y^*) & \frac{\partial g}{\partial y_n}(x^*, y^*) \end{pmatrix}$$

Be the Jacobian matrix of $\binom{f}{g}, evaluated\ at\ (x^*, y^*)$, then (x^*, y^*) is stable if all eigenvalues of J have magnitude less than one; (x^*, y^*) is unstable if at least one of the eigenvalues has magnitude greater than one;

- Eigenvalues λ of J are obtained from the characteristic equation $\det(J - \lambda I) = 0$ Where I denotes the identity matrix
- Magnitude of a real eigenvalue is absolute value, while magnitude of a complex eigenvalue $|a + bi| = \sqrt{a^2 + b^2}$
- This stability theorem can be easily extended to a higher dimensional system. For a system of m difference equations, the Jacobian matrix will be m x n, and there will be m eigenvalues (counting multiplicity).
- For a two-dimensional system, the characteristic equation $\det(J - \lambda I) = 0$ is equivalent to $\lambda^2 - (\mathrm{tr}\, J)\lambda + \det J = 0$. We can show that $|tr\, J| < 1 + \det J < 2$ are sufficient and necessary conditions for all eigenvalues of J to have the magnitude less than one, them the equilibrium (x^*, y^*) is stable.

If additionally $(\mathrm{tr}\, J)^2 - 4 \det J > 0$, then (x^*, y^*) is a stable node (real eigenvalues);

If additionally $(\mathrm{tr}\, J)^2 - 4 \det J < 0$, then (x^*, y^*) is a stable spiral (complex eigenvalues);

We can apply the above definition and theorem to analysis in discrete -time systems.

III. Model Description

Let the total population density of any area be σ = (N + P), where P represent the actual population and N represent the new migrated young adult entrants into the population, therefore the population can be broken-down into four groups, namely, the number of vaccinated person V(t), the susceptible S(t), the infected I(t) and the recovered R(t) (people who has successful cure of infection), the proportion ϕ of new young immigrant adult entrants were vaccinated BCG for the protection against infection. So the immunized part of the population changes due to the coming in of the vaccinated young adult into the population. This vaccinated group V (t) of the population reduces due to the expiration of duration of vaccine efficacy at the rate δ and natural death rate μ,

For the susceptible group population S (t) inflates due to non-vaccinated young adult entrants at the rate (1- ϕ) σ and the expiration of duration of vaccine efficacy at the rate δ. The susceptible population also diminishes due to natural death μ and the infection with an incident rate of infection β. Rate of death caused by chronic disease α. The rate of immediate incident of infection caused by contacts of member of susceptible group with infectious group β, successful cure of infectious patients at the rate γ, the non-vaccinated person at the rate Є and also reduces by natural death rate μ.

Lastly the recovered group R (t) increases due to successful cure of infectious patients at the rate γ and reduces by natural death rate μ.

The Model diagram of the system as follows:

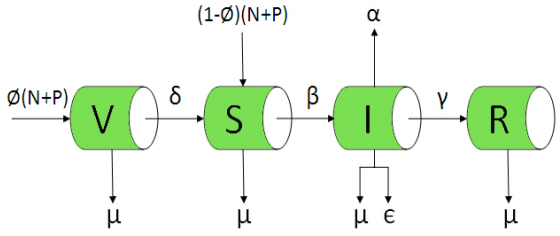

Fig.1 Model diagram of VSIR

Group 1: The rate of change of vaccination yields

$$\frac{dV}{dt} = \sigma\phi - (\delta + \mu)V \quad (1)$$

The model equations for the disease free equilibrium states: If $\frac{dV}{dt} = 0$, then the system of Equilibrium Eq. (1) becomes:

$$\sigma\phi - (\delta + \mu)V = 0 \quad (2)$$

Group 2: The rate of change of susceptible in the population can be represented as

$$\frac{dS}{dt} = (1-\phi)\sigma + \delta V - \beta SI - \mu S \quad (3)$$

If $\frac{ds}{dt}$ =0, then the system of Equilibrium Eq. (3) becomes:

$$(1-\phi)\sigma + \delta V - \beta SI - \mu S = 0 \quad (4)$$

Group 3: The rate of change of infectious group of population yield

$$\frac{dI}{dt} = S\beta I - (\gamma + \mu + \alpha + \epsilon)I \quad (5)$$

If $\frac{dI}{dt} = 0$, then the system of Equilibrium (5) becomes:

$$S\beta I - (\gamma + \mu + \alpha + \epsilon)I = 0 \quad (6)$$

Group4: The change in recovered group R (t) given below;

$$\frac{dR}{dt} = \gamma I - \mu R \quad (7)$$

If $\frac{dR}{dt} = 0$, then the system of Equilibrium (7) becomes:

$$\gamma I - \mu R = 0 \quad (8)$$

From (6) we have

$$I = 0 \quad (9)$$

and

$$S\beta - \gamma - \mu - \alpha - \epsilon = 0 \quad (10)$$

Substituting (9) for I in (8), we get:

$$R = 0 \quad (11)$$

From (2)

$$V = \frac{\sigma\phi}{\delta+\mu} \quad (12)$$

Substituting (9) and (12) for I and V in (4) becomes:

$$S = \frac{\delta\sigma + \mu(1-\phi)\sigma}{\mu(\delta+\mu)} \quad (13)$$

Hence the disease free equilibrium state is, by replacing σ = (N+P) we have:

$$[V, S, I, R] = \left(\frac{(N+P)\phi}{\delta+\mu}, \frac{\delta(N+P) + \mu(1-\phi)(N+P)}{\mu(\delta+\mu)}, 0, 0\right)$$

From (10)

$$S = \frac{\gamma+\mu+\alpha+\epsilon}{\beta} \quad (14)$$

From (6)

$$I = \frac{(1-\phi)\sigma + \delta V - \mu S}{\beta S} \quad (15)$$

Substituting (12) and (14) for V and S in (15), we get

$$I = \frac{(\delta+\mu)[\sigma\beta - \mu(\gamma+\mu+\alpha+\epsilon)] - \phi\sigma\mu\beta}{\beta(\delta+\mu)[\gamma+\mu+\alpha+\epsilon]} \quad (16)$$

Substituting (16) for I in (08), we get:

$$R = \frac{\gamma\{(\delta+\mu)[\sigma\beta - \mu(\gamma+\mu+\alpha+\epsilon)] - \phi\sigma\mu\beta\}}{\mu\beta(\delta+\mu)[\gamma+\mu+\alpha+\epsilon]} \quad (17)$$

Hence, the system of endemic equilibrium state becomes;

$$\left.\begin{aligned} V &= \frac{\sigma\phi}{\delta+\mu} \\ S &= \frac{\gamma+\mu+\alpha+\epsilon}{\beta} \\ I &= \frac{\sigma\phi + \delta V - \mu S}{\beta S} \\ R &= \frac{\gamma\{(\delta+\mu)[\sigma\beta - \mu(\gamma+\mu+\alpha+\epsilon)] - \phi\sigma\mu\beta\}}{\mu\beta(\delta+\mu)[\gamma+\mu+\alpha+\epsilon]} \end{aligned}\right\} \quad (18)$$

Stability Analysis of the disease free equilibrium states,

$$\left.\begin{aligned} \sigma\phi - (\delta+\mu)V &= 0 \\ \sigma\phi + \delta V - \beta SI - \mu S &= 0 \\ S\beta I - (\gamma+\mu+\alpha+\epsilon)I &= 0 \\ \gamma I - \mu R &= 0 \end{aligned}\right\} \quad (19)$$

The Jacobean matrix of the transformed from Eq. (19), can be represented as:

$$J = \begin{bmatrix} \underline{V} & \underline{S} & \underline{I} & \underline{R} \\ -(\delta+\mu) & 0 & 0 & 0 \\ \delta & -(\beta I + \mu) & -\beta S & 0 \\ 0 & \beta I & (\beta S - \gamma - \mu - \alpha - \epsilon) & 0 \\ 0 & 0 & \gamma & -\mu \end{bmatrix}$$

The characteristic equation is obtained from the Jacobean determinant with the Eigen values λ.

$$\det((J-\lambda I)=\det\begin{bmatrix}-(\delta+\mu+\lambda) & 0 & 0 & 0\\ \delta & -(\beta I+\mu+\lambda) & -\beta S & 0\\ 0 & \beta I & (\beta S-\gamma-\mu-\alpha-\epsilon-\lambda) & 0\\ 0 & 0 & \gamma & -(\mu+\lambda)\end{bmatrix}$$

$$=-(\delta+\mu+\lambda)\det\begin{bmatrix}-(\beta I+\mu+\lambda) & -\beta S & 0\\ \beta I & (\beta S-\gamma-\mu-\alpha-\epsilon-\lambda) & 0\\ 0 & \gamma & -(\mu+\lambda)\end{bmatrix} \quad (20)$$

At the disease free equilibrium state substituting the value of I = 0 in (18).

$$-(\delta+\mu+\lambda)\det\begin{bmatrix}-(\mu+\lambda) & -\beta S & 0\\ 0 & (\beta S-\gamma-\mu-\alpha-\epsilon-\lambda) & 0\\ 0 & \gamma & -(\mu+\lambda)\end{bmatrix}=0$$

Therefore,

$$-(\delta+\mu+\lambda)[-(\mu+\lambda)\{-(\mu+\lambda)(\beta S-\gamma-\mu-\alpha-\epsilon-\lambda)\}]=0$$

$$-(\delta+\mu+\lambda)\,[(\mu+\lambda)^2(\,\beta S-\gamma-\mu-\alpha-\epsilon-\lambda)]=0 \quad (21)$$

$$-(\delta+\mu+\lambda)\;=0 \quad (22)$$

$$[\,\beta S-\gamma-\mu-\alpha-\epsilon-\lambda]=0 \quad (23)$$

$$(\mu+\lambda)^2\;=0 \quad (24)$$

Substituting (13) for S in (23), we get:

$$\left[\frac{\beta\{\delta\sigma+\mu(1-\phi)\sigma\}}{\mu(\delta+\mu)}-(\gamma+\mu+\alpha+\epsilon+\lambda)\right]=0 \quad (25)$$

From (24)

$$(\mu+\lambda)^2=0$$
$$\lambda_1=\lambda_2=-\mu \quad (26)$$

In (25) the negative sign shows that the natural death rate μ is increasing.

$$\lambda_3=-(\delta+\mu) \quad (27)$$

In (27) the Eigen value of λ_3 is also negative this shows that the expiration of efficacy of vaccination at the rate δ is increase and the susceptible population is also diminished due to the natural death rate μ.

From (25) replacing λ by λ_4

$$\lambda_4=\frac{\beta\{\delta\sigma+\mu(1-\phi)\sigma\}}{\mu(\delta+\mu)}-(\gamma+\mu+\alpha+\epsilon) \quad (28)$$

Since λ_1,λ_2, and λ_3 are negative indicates that λ_4 should also be negative; the disease free equilibrium state will be stable. If $\frac{\beta\{\delta\sigma+\mu(1-\phi)\sigma\}}{\mu(\delta+\mu)}<(\gamma+\mu+\alpha+\epsilon)$; by replacing σ = (N+P) we have $\frac{\beta\{\delta(N+P)+\mu(1-\phi)(N+P)\}}{\mu(\delta+\mu)}<(\gamma+\mu+\alpha+\epsilon)$.

IV. Result and Discussion

The disease stability analysis is carried out by the following equations.

$$\lambda_1=\lambda_2=-\mu$$
$$\lambda_3=-(\delta+\mu)$$
$$\lambda_4=\frac{\beta\{\delta(N+P)+\mu(1-\phi)(N+P)\}}{\mu(\delta+\mu)}-(\gamma+\mu+\alpha+\epsilon)$$

For the disease free equilibrium state (i.e. the state of complete eradication of TB) to be stable, when all the Eigen values λ_1,λ_2 and λ_3 are negative, whereas the fourth Eigen value λ_4 must also be negative which is possible under this condition:

$$\frac{\beta\{\delta(N+P)+\mu(1-\phi)(N+P)\}}{\mu(\delta+\mu)}<(\gamma+\mu+\alpha+\epsilon) \quad (29)$$

here, left hand side term of (29) denotes the number of dormant infections produced, in addition it also exhibit the effect of BCG vaccine on number of young adult produced against all forms of TB. However, (γ+μ+α+ϵ) is total removal rate from the infectious group The above inequality shows that the total removal rate from infectious group should be greater than the total number of dormant infections produced throughout the infectious group .and probability that persons who are not vaccinated due to the infection throughout the infectious group.

Moreover, the effect of BCG vaccine has been discussed against all forms of TB and the variations in the protective efficacy of BCG widely accepted among young adult person.

V. Conclusion

In this study mathematical model has been constructed to quantify effect of BCG vaccine to protect the immigrant young adult persons and the disease stability analysis has been developed. The stability analysis is carried out. The following model equations are used to achieve the objectives.

$$\lambda_1=\lambda_2=-\mu$$
$$\lambda_3=-(\delta+\mu)$$
$$\lambda_4=\frac{\beta\{\delta(N+P)+\mu(1-\phi)(N+P)\}}{\mu(\delta+\mu)}-(\gamma+\mu+\alpha+\epsilon)$$

Eq. (29) shows that the total removal rate from the infectious group should be greater than total number of dormant infections produced throughout infectious period. In order to attain steadiness of model four computed Eigen values has been used. Beside its negative sign confirm the absolute suppression of tuberculosis. Whereas inequalities condition for fourth Eigen values demonstrated that the total removal rate of infectious state should be greater than the number of young person who are immunized inhabitants in the total number of infectious produced with the probability that person who are not vaccinated due to the contagion throughout the infectious group. It has also been noted that for population to be persistent if and only if recovery rate from the infectious group must be greater than the natural rate of death. Infection

rate of death join mutually $\mu+\alpha$ whereas probability death rate for all non-vaccinated natives is ϵ further the population will be inclined towards annihilation.

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