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Effect of Vaccination, Treatment and Population Area Size on the Transmission Dynamics of Tuberculosis in a Proportionate Mixing Population

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Abstract: We have examined the effect of vaccination, treatment and population area size on the transmission dynamics of tuberculosis, in a proportionate mixing population with vital dynamics, where the vaccine is assumed to be leaking, so that vaccinated individuals progress to the infectives population, when in contact with the disease. Three subs-models for the transmission dynamics of the disease are proposed and the influence of the population area size on each are examined via the basic reproductive number of the disease and the determinant, trace stability conditions. The non trivial equilibrium states are obtained and their stability discussed.

Key words: Equilibrium state, stability, vital dynamics, population density, population area size

INTRODUCTION

There has been rising cases of tuberculosis related death in recent times. According to the world health report, about a third of the world's population is affected by tuberculosis, (Mugisha *et al*., 2005). Mostly affected are the third world countries, where 99% tuberculosis related death occurs. Also out of 1.7 billion people estimated to be infected with tuberculosis in the world, 1.3 billion of them live in developing countries, (Mugisha *et al*., 2005). It has been observed in most epidemiological studies that tuberculosis is often as a result of poverty and underdevelopment. It occurs in the most socioeconomically deprived sectors, where factors contributing to its spread exist in overcrowding, malnutrition and lack of access to good health care services, (Mugisha *et al*., 2005). There is no doubt that, Nigeria and others developing countries experiences is not different. Most communities in Nigeria are ravaged by poverty, lack of good health care services and other facilitating environmental factors exist, contributing to the spread of the disease. The pattern of distribution of population is often unevenly, such that there are many people in small areas, while others much large areas have sparsely concentration of people, (Reuben K. Udoh, 2003). This massive concentration of people in a limited area is a major factor which has helped to sustain some diseases, especially the airborne diseases of which tuberculosis is one. In this study we examined the role of the population area size on an S-V-I-T-R and the sub-models, S-V-I-R, S-I-T-R, S-I-R, where S, V, I, T and R are population densities.

The model equation: A lot of works have done by researchers in providing vaccination and treatment models for infectious diseases. Some of which can be seen in the work of Murray (1989), Leah Edelstein (2005) and age structured approach by Metz and Diekmann (2005), Hsieh (1996), provided treatment model for HIV in a varying population (Mugisha *et al*., 2005), provided a treatment model for the dynamics of tuberculosis in a density dependent population and others. It is obvious that both treatment and vaccination play an important part in the prevention, control and management of tuberculosis. Assume there is a constant hereditary recruitment of infectious into the infectious population and a birth rate same as death rate for all population and that Vaccinated susceptibles can progress into infectives p opulation due to the leaking of the vaccine, so that the susceptible can equally progress to the infectious population through contact with an infective.

The infectives are then removed, when not treated, until death, while the treated progress to the susceptible population, where they either chose to be vaccinated or not.

The following parameters are represented as follows:

β_1 : Probability of transmission of Tuberculosis from an infectious person, not vaccinated to a susceptible person.
β_2 : Probability of transmission of tuberculosis form an infectious person to a susceptible not vaccinated.
σ : The rate at which susceptibles are vaccinated.
μ : Natural mortality and birth rates

ρ : Hereditary recruitment into the infecives population.
k_1 : Treatment rate for infectives
k_2 : Recovery rate.
τ : Disease induced mortality rate.
m : Rate of removal of infectives
c : Per capital contact rate
S : Population density of the susceptibles.
I : Population density of the infectives.
V : Population density of the vaccinated.
T : Population density of the treated.
A : The total area occupied by the population

Using above definitions and assumptions in a proportionate mixing population, the density dependent dynamics of tuberculosis are described by the following equations,

$$\begin{aligned}
\dot{S} &= \Delta - \frac{1}{A}c\beta_1 IS - (\sigma+\mu)S \\
\dot{V} &= \sigma S - \frac{1}{A}c\beta_2 IV - \mu V \\
\dot{I} &= \rho + \frac{1}{A}c(\beta_1 S + \beta_2 V)I - \mu S - (\mu + k_1)I \\
\dot{T} &= k_1 I - (k_2+\mu)T \\
\ddot{R} &= mI - (\tau+\mu)R
\end{aligned} \tag{2.1}$$

Where N = S + V +I +T + R., is the total population size. At disease-free equilibrium state, we have

$$S=S_0=\frac{\Delta}{\sigma+\mu} \quad \text{and}$$

$$I = R = T = 0, \quad V = \frac{\Delta}{\mu}(\frac{\sigma}{\sigma+\mu}).$$

The Jacobian matrix at this state is,

$$J_{E_0} = \begin{pmatrix}
-(\sigma+\mu), & 0 & \frac{1}{A}c\beta_1(\frac{1}{\sigma+\mu})\Delta & 0 & 0 \\
\sigma & -\mu & -\eta & 0 & 0 \\
-\mu & 0 & \omega & 0 & 0 \\
0 & 0 & k_1 & -(k_2+\mu) & 0 \\
0 & 0 & m & \sigma & -(\tau+\mu)
\end{pmatrix}$$

Where

$$\eta = \frac{1}{A}c\beta_2[\frac{\Delta}{\mu}(\frac{\sigma}{\sigma+\mu})],$$

$$\omega = \frac{1}{A}[c\beta_1(\frac{1}{\sigma+\mu})\Delta + c\beta_2\frac{\Delta}{\mu}(\frac{\sigma}{\sigma+\mu})] - (m+k_1).$$

$$(\mu+\lambda)(\tau+\mu+\lambda)(k_2+\mu+\lambda)\det\begin{pmatrix}
(-(\sigma+\mu+\lambda) & \frac{1}{A}c\beta_1(\frac{1}{\sigma+\mu})\Delta \\
-\mu & \omega-\lambda
\end{pmatrix} = 0$$

Where λ_j, are the eigenvalues of the jacobian matrix. Let matrix C =

$$\begin{pmatrix}
-(\sigma+\mu) & \frac{1}{A}c\beta_1(\frac{1}{\sigma+\mu})\Delta \\
-\mu & \omega
\end{pmatrix}.$$

We have,

$$\begin{aligned}
\det C &= \frac{1}{A}c\beta_1(\frac{\mu}{\sigma+\mu})\Delta - (\sigma+\mu)\omega \\
&\frac{1}{A}c\beta_1(\frac{\mu}{\sigma+\mu})\Delta + (k_1+m)(\sigma+\mu) - \\
&\frac{1}{A}[c\beta_1(\frac{1}{\sigma+\mu})\Delta + c\beta_2(\frac{\sigma}{\sigma+\mu})\frac{\Delta}{\mu}].
\end{aligned}$$

While the trace C =

$$\begin{aligned}
\omega - (\sigma+\mu) &= \frac{1}{A}[c\beta_1(\frac{1}{\sigma+\mu})\Delta + \\
&c\beta_2(\frac{\sigma}{\sigma+\mu})\frac{\Delta}{\mu} - (k_1 + +m+\mu+\sigma).
\end{aligned}$$

The determinant of matrix C is positive, while the trace is negative when,

$$\frac{1}{A}[c\beta_1(\frac{1}{\sigma+\mu})\Delta + c\beta_2\frac{\Delta}{\mu}(\frac{\sigma}{\sigma+\mu}) < (k_1+m+\mu+\sigma)$$

or when

$$\begin{aligned}
A > c\beta_1(\frac{1}{\sigma+\mu})(\frac{\Delta}{k_1+m+\mu+\sigma}) + \\
c\beta_2\frac{\Delta}{\mu}(\frac{\sigma}{\sigma+\mu})(\frac{1}{k_1+m+\mu+\sigma})
\end{aligned}$$

Dividing through by $\frac{\Delta}{\sigma+\mu}$

we have,

$$\left(\frac{A}{\Delta/\sigma+\mu}\right) > c\beta_1\left(\frac{1}{k_1+m+\mu+\sigma}\right) + c\beta_2\left(\frac{1}{k_1+m+\mu+\sigma}\right)\frac{\sigma}{\mu} \quad (2.2)$$

$\left(\frac{A}{\Delta/\sigma+\mu}\right)$ is the area occupied per individual, or characteristic area,. The critical area size requires for eradication of tuberculosis in the population is,

$$c\beta_1\left(\frac{1}{k_1+m+\mu+\sigma}\right) + c\beta_2\left(\frac{1}{k_1+m+\mu+\sigma}\right)\frac{\sigma}{\mu} \quad (2.3)$$

The disease free equilibrium state is locally asymptotically stable if these conditions are met. Also for minimum disease incidence, we require the infectious and the removed population sizes to decrease. This is attained when I, R<0, We would then have,

$$\frac{1}{A}c\beta_1 IS + \frac{1}{A}c\beta_2 IV < \mu S + (\mu + k_1)I - \rho$$

and mI <(τ+μ) R, combining the two equation, we have,

$$\left(\frac{R}{m}\right)\frac{(\tau+\mu)[c\beta_1 S + c\beta_2 V]}{\mu S - \rho + (k_1+\mu)\frac{R}{m}(\tau+\mu)} < A$$

to minimize the incidence of tuberculosis in the population. Using the basic reproductive number, R_0, we examined the stability of the disease-free equilibrium in line with Herfferman *et al*. (2005), Mugisha *et al*. (2005), Castillo-Chavez where R_0 is the spectral radius (dominant eigenvalue) of the matrix MD^{-1}, M ≥ and D > 0, is diagonal matrix. Let X = (S, V, T), Z = (I, R) and the disease free equilibrium state as,

$$E_0 = \left(\frac{\Delta}{\sigma+\mu}, \quad \frac{\Delta}{\mu}\left(\frac{\sigma}{\sigma+\mu}\right), \quad 0, 0, 0\right).$$

We then have,

$$\dot{X} = \Delta + \sigma X - \frac{1}{A}[c\beta_1 + c\beta_2]$$
$$XZ - (\sigma+\mu)X - \mu X + k_1 Z - (k_2+\mu)Z = f(X,Z)$$
$$\dot{Z} = \rho + \frac{1}{A}[c\beta_1 + c\beta_2]\frac{\Delta}{\sigma-\mu}Z - \mu\frac{\Delta}{\sigma-\mu} -$$
$$k_1 Z - (\tau+\mu)Z = h(X^*,Z)$$

Also

$$\dot{h}(X^*,Z) = \frac{1}{A}[c\beta_1 + c\beta_2]\frac{\Delta}{\sigma+\mu} - (k_1+\tau+\mu).$$

Then matrix H = $\frac{\partial h}{\partial Z}$ = M-D. Thus, we have,

$$M = \frac{1}{A}[c\beta_1 + c\beta_2]\frac{\Delta}{\sigma+\mu},$$

and H = (k_1 + τ + μ). The basic reproductive number can then be defined as,

$$R_0 = \rho(MD^{-1}) = \left(\frac{\Delta/\sigma+\mu}{A}\right)\frac{(\beta_1+\beta_2)c}{k_1+\tau+\mu},$$

$\beta_1 c$ and $\beta_2 c$ are the effective transmission rates.

$$\frac{1}{k_1+\tau+\mu}$$

is the effective infectious period and

$$\frac{(\Delta/\sigma+\mu)}{A}$$

is the density of the susceptibles. The disease free equilibrium state is locally asymptotically stable if $R_0 < 1$ and is unstable if $R_0 > 1$., in this case the endemic state is asymptotically stable and the infection will not be destroyed but spread in the population. Using these definitions, we would have the following,
When $R_0 < 1$, we have,

$$\left(\frac{\Delta/\sigma+\mu}{A}\right)\frac{(\beta_1+\beta_2)c}{k_1+\tau+\mu} < 1$$

meaning that

$$\left(\frac{A}{\Delta/(\sigma+\mu)}\right) > \frac{(\beta_1+\beta_2)c}{k_1+\tau+\mu}.$$

Also when R_0 >1, we have

$$\left(\frac{\Delta/\sigma+\mu}{A}\right) > \frac{(\beta_1+\beta_2)c}{k_1+\tau+\mu}$$

Sub- model without treatment, $k_1 = 0, \sigma \neq 0$: We have the sub- model equations as,

$$\dot{S} = \Delta - \frac{1}{A}c\beta_1 IS - (\sigma + \mu)S$$

$$\dot{V} = \sigma S - \frac{1}{A}c\beta_2 IV - \mu V$$

$$\dot{I} = \frac{1}{A}c\beta_1 IS + \frac{1}{A}c\beta_2 IV + \rho - \mu S - mI$$

$$\dot{R} = mI - (\tau + \mu)R$$

The disease free equilibrium state is,

$$E_0 = (\frac{\Delta}{\sigma + \mu}, \quad \frac{\Delta}{\mu}(\frac{\sigma}{\sigma + \mu}), \quad 0, \quad 0)$$

and the Jacobian at the disease free equilibrium state is,

$$J_{E_0} = \begin{pmatrix} -(\mu+\sigma), & 0 & -\frac{1}{A}c\beta_1(\frac{\Delta}{\sigma+\mu}) & 0 \\ \sigma & -\mu & -\frac{1}{A}c\beta_2(\frac{\sigma}{\sigma+\mu})(\frac{\Delta}{\mu}) & 0 \\ 0 & 0 & \frac{c}{A}(\frac{\Delta}{\sigma+\mu})[\beta_1 + \beta_2 \sigma/\mu] - m & 0 \\ 0 & 0 & m & -(\tau+\mu) \end{pmatrix}$$

if λ_j, are the eigenvalues of matrix J_{E0}, then we have,

$$(\tau+\mu+\lambda)(\mu+\lambda)\det \begin{pmatrix} -(\mu+\sigma+\lambda) & -\frac{1}{A}c\beta_1(\frac{\Delta}{\sigma+\mu}) \\ 0 & \frac{c}{A}(\frac{\Delta}{\sigma+\mu})[\beta_1 + \beta_2 \sigma/\mu] - (m+\lambda) \end{pmatrix} = 0$$

$$\text{Let } M = \begin{pmatrix} -(\mu+\sigma) & -\frac{1}{A}c\beta_1(\frac{\Delta}{\sigma+\mu}) \\ 0 & \frac{c}{A}(\frac{\Delta}{\sigma+\mu})[\beta_1 + \beta_2 \sigma/\mu] - m \end{pmatrix}$$

Then, the determinant of matrix

$$M = m(\mu+\sigma) - m(\frac{\Delta/\sigma+\mu}{A})[c\beta_1 + c\beta_2 \Delta/\mu]$$

and the trace of matrix

$$M = (\frac{\Delta/\sigma+\mu}{A})[c\beta_1 + c\beta_2 \Delta/\mu] - (\mu+\sigma)$$

The determinant of matrix M is positive only when

$$m(\mu+\sigma) > m(\frac{\Delta/\sigma+\mu}{A})[c\beta_1 + c\beta_2 \Delta/\mu]$$

and the trace is negative when

$$(\frac{\Delta/\sigma+\mu}{A})[c\beta_1 + c\beta_2 \Delta/\mu] < (\mu+\sigma).$$

Thus, the local stability of the equilibrium state E_0 holds if these conditions are satisfied. This is achieved when the population area size A, is large enough.

Sub- model without vaccination $\sigma = 0, k_1 \neq 0$: We have the sub- model equation for the transmission dynamics as,

$$\dot{S} = \Delta - \frac{1}{A}c\beta IS - \mu S$$

$$\dot{I} = \frac{1}{A}c\beta IS + \rho - \mu S - (\mu + k_1)$$

$$\dot{T} = k_1 I - (k_2 + \mu)T$$

$$\dot{R} = mI - (\tau + \mu)R$$

The disease free equilibrium state

$$E_0 = (\frac{\Delta}{\mu}, \quad 0, \quad 0, \quad 0)$$

and the Jacobian matrix at this state is

$$J_{E_0} = \begin{pmatrix} -\mu & -\frac{1}{A}c\beta(\frac{\Delta}{\mu}) & 0 & 0 \\ -\mu & \frac{1}{A}c\beta(\frac{\Delta}{\mu}) - (m+k_1) & 0 & 0 \\ 0 & k_1 & -(k_2+\mu) & 0 \\ 0 & m & 0 & -(\tau+\mu) \end{pmatrix}$$

Also,

$$(\tau+\mu+\lambda)(k_2+\mu+\lambda)\det \begin{pmatrix} -(\mu+\lambda) & -\frac{1}{A}c\beta(\frac{\Delta}{\mu}) \\ -\mu & \frac{1}{A}c\beta(\frac{\Delta}{\mu}) - (\mu+k_1+\lambda) \end{pmatrix} = 0$$

Where λ_j, are the eigenvalues of matrix J_{E0}.

$$\text{Let } M=\begin{pmatrix} -\mu & -\frac{1}{A}c\beta(\frac{\Delta}{\mu}) \\ -\mu & \frac{1}{A}c\beta(\frac{\Delta}{\mu})-(\mu+k_1) \end{pmatrix}$$

The determinant of matrix

$$M=\mu[(k_1+m)-2c\beta(\frac{\Delta/\mu}{A}).$$

This positive when

$$\mu(k_1+m)>2c\beta(\frac{\Delta/\mu}{A}),$$

and A is large enough. Also the trace of Matrix

$$M=c\beta(\frac{\Delta/\mu}{A})-(m+k_1).$$

This negative when

$$c\beta(\frac{\Delta/\mu}{A})<m+k_1$$

and A large enough.
Thus large population area size will give a stable disease free equilibrium state.

Sub-model without treatment and vaccination, $\sigma = k_1 = 0$:
We then have the model Equation as,

$$\dot{S}=\Delta-\frac{1}{A}c\beta IS-\mu S$$

$$\dot{I}=\frac{1}{A}c\beta IS+\rho-\mu S-mI$$

$$\dot{R}=mI-(\tau+\mu)R$$

The disease free equilibrium state is $E_0=(\frac{\Delta}{\mu},\ 0,\ 0\ )$

and the Jacobian matrix

$$J_{E_0}=\begin{pmatrix} -\mu & 0 & 0 \\ -\mu & -\frac{1}{A}c\beta(\frac{\Delta}{\mu})-m & 0 \\ 0 & m & -(\tau+\mu) \end{pmatrix}$$

Also,

$$-(\tau+\mu+\lambda)\det\begin{pmatrix} -(\mu+\lambda) & 0 \\ -\mu & \frac{1}{A}c\beta(\frac{\Delta}{\mu})-(m+\lambda) \end{pmatrix}=0$$

Where λ are the eigen values of matrix J_{E0}.

$$\text{Let } M=\begin{pmatrix} -\mu & 0 \\ -\mu & \frac{1}{A}c\beta(\frac{\Delta}{\mu})-m \end{pmatrix}$$

Then the determinant and trace of matrix M are,

$$\det M=m\mu-\frac{1}{A}c\beta(\frac{\Delta}{\mu})$$

and trace of

$$M=c\beta(\frac{\Delta/\mu}{A})-(m+\mu)$$

Stability of disease free equilibrium state is depended on whether, the determinant of M is positive and the trace of M is negative. However the determinant is positive and trace negative if the population area size is sufficiently large as in other cases. Thus the DFE is asymptotically stable if the population area size is large enough.

CONCLUSION

We have clearly seen the impact of vaccination and treatment as control and management therapies for tuberculosis infection and influence of population area size on the transmission dynamics of the diseases. We have also observed that for stability of the disease free equilibrium state, the population area size should be large enough for all cases, whether treatment and vaccination is practiced o r not and that the characteristic area should be greater than

$$(\frac{1}{k_1+m+\mu+\sigma})[c\beta_1+c\beta_2\frac{\sigma}{\mu}]$$

The density of the susceptibles, $(\frac{\Delta/\sigma+\mu}{A})$,is influenced by the size of the population area, A occupied. That if the area is big, then the density of the susceptible will be small, thus reducing the size of the basic reproductive

number. This is the desired target of any intervention therapy for disease eradication. If the area A, is small, then the density of the susceptibles will be higher and consequently the basic reproductive number and infection generated by a single infectious individual will be higher. Thus, there is need for the population to have large population area size and also employed vaccination and treatment of the infectious individuals. This will help eradicate the disease in the population completely.

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