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Research paper

Analysis of a tuberculosis model with undetected and lost-sight cases

D.P. Moualeu[a,c], A. Nana Yakam[b,c], S. Bowong[b,c,*], A. Temgoua[b]

[a] Institute for Horticultural Production Systems, Vegetable Systems Modelling Section, Faculty of Natural Sciences, Leibniz Universität Hannover, Herrenhäuser Str. 2, Hannover D-30419, Germany
[b] Department of Mathematics and Computer Science, Faculty of Science, University of Douala, PO Box 24157, Douala, Cameroon
[c] UMI 209 IRD/UPMC UMMISCO, Bondy, France and Project-Team GRIMCAPE, LIRIMA and The African Center of Excellence in Information and Communication Technologies (CETIC), University of Yaounde I, Cameroon

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ABSTRACT

A deterministic model of tuberculosis (TB) in sub-Saharan Africa including undetected and lost-sight cases is presented and analyzed. The model is shown to exhibit the phenomenon of backward bifurcation, when a stable disease-free equilibrium co-exists with one or more stable endemic equilibrium points when the associated basic reproduction number ($\mathcal{R}_0$) is less than unity. Analyzing the model obviously reveals that exogenous reinfection plays a key role on the existence of backward bifurcation. However, an analysis of the ranges of exogenous reinfection suggested that backward bifurcation occurs only for very high and unrealistic ranges of the exogenous reinfection rate. Random perturbation of reinfection rates was performed to gain insight into the role of this latter on the stability of the disease free equilibrium.

1. Introduction

The global burden of tuberculosis (TB) has increased over the past two decades, despite widespread implementation of control strategies including BCG (Bacillus Calmette-Guerrin) vaccination and the World Health Organization's (WHO) DOTS strategy which focuses on case finding and short-course chemotherapy cause of death. TB is the second largest cause of death from an infectious agent after HIV/AIDS in developing countries [19]. In the modern era, TB is recognized as a disease that preys upon social disadvantage [7,8]. It remains a worldwide emergency mostly affecting poor countries and to this old and persistent threat, the multidrug-resistant TB is an emergency adding further challenges. Despite predictions of a decline in global incidence, the number of new cases continues to grow, approaching 10 million in 2010 [20].

TB has a latent or incubation period during which the individual is said to be infected but not infectious. This period was modeled either by incorporating as a delay effect or by introducing an exposed class. Therefore, second infection or reinfection occurs in an individual in both high and low-incidence regions, which is already experiencing an infection with another agent. This parameter plays an important role on TB dynamics.

Some authors proposed mathematical models of TB including reinfection and assumed that the rate of reinfection is a multiple of the rate of first infection [5,22,29,45,47–49,52]. Exposed individuals who have been previously infected (in

* Corresponding author at: Department of Mathematics and Computer Science, Faculty of Science, University of Douala, PO Box 24157, Douala, Cameroon. Tel.: +237 678 00 97 81.
E-mail address: sbowong@gmail.com (S. Bowong).

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dormant stage) or recovered individuals may acquire new infection from another infectious individual due to low immunity of persons. Therefore, individuals in the latent stage of TB progress into active stage due to exogenous reinfection and recovered individual may progress to Latently infected class [5,22,29,45,47–49,52]. Studies confirmed that reinfection in areas with a low incidence of tuberculosis is possible, although less common than in high-incidence geographical regions, indicating that higher prevalence of *M. tuberculosis* represents the major risk for tuberculosis reinfection.

The challenge of TB control in developing countries is due to the increase of TB incidence by a high level of undiagnosed infectious population and lost sight population with respect to diagnosed infectious cases. Undiagnosed infectious population means people who have not yet been to a hospital for diagnosis or have not been detected, but have a pulmonary TB [4,51] when lost sight population are people who have been diagnosed as having active TB, begun their treatment and quitted before the end. Lost-sight population are the most likely to develop multi-drug resistance [50]. Compared to existing results [1,3,9,15,18,22,32,38,43] and references therein, our work differs from these studies in that our model, in addition to undiagnosed infectious and lost sight population, also considers the aspects of exogenous reinfections, disease relapse as well as primary active TB cases, natural recovery and traditional medicine or self-medication (practiced in Sub-Saharan Africa). Also, it is recognized that undiagnosed population, lost sight population and exogenous reinfections are important components of TB transmission in Sub-Saharan Africa. For the new mathematical model, the infective class is divided into three subgroups with different properties: (i) diagnosed infectious population, (ii) undiagnosed infectious population and (iii) lost sight population. According to the National Committee of Fight against TB of Cameroon (NCFT) [40], about 8% of diagnosed infectious that begin their therapy treatment never returned to the hospital for the rest of sputum examinations and treatment, and then become lost sight. This class of TB epidemiological models can be extended to many classes of infective individuals and data for many other African countries.

For many epidemiological models, a threshold condition that indicates whether an infection introduced into a population will be eliminated or become endemic was defined [13]. The basic reproduction number $\mathcal{R}_0$ is defined as the average number of secondary infections produced by an infected individual in a completely susceptible population [24]. In models with only two steady states and a transcritical bifurcation, $\mathcal{R}_0 > 1$ implies that the endemic state is stable (e.g., the infection persists), and $\mathcal{R}_0 \leq 1$ implies that the uninfected state is stable (e.g., the infection will die out). The co-existence of disease-free equilibrium and endemic equilibrium points when the basic reproduction number ($\mathcal{R}_0 < 1$) is typically associated with the backward or subcritical bifurcation. This phenomenon was found in many epidemiological settings (see for instance, [21,23,30,44] and references therein). The epidemiological implication of is that the classical requirement of having the associated reproduction number less than unity, while necessary is not a sufficient condition for disease control. Results showed that a threshold level of reinfection exists in all cases of the model. Beyond this threshold, the dynamics of the model are described by a backward bifurcation. However, uncertainty analysis of the parameters showed that this threshold is too high to be attained in a realistic epidemic [44]. In our previous works, we analyzed optimal control strategies for the model and estimated parameters corresponding to data recorded in Cameroon [35–37]. Here, we intend to discuss the role of exogenous reinfection on the existence of backward bifurcation in the TB model. In this paper, we determine the basic reproduction ratio, and discuss the existence and the stability of the endemic equilibrium and the disease free equilibrium (DFE). Some discussion about the TB persistence condition was deduced.

2. The proposed model

2.1. The model formulation

A finite total population at time t denoted by $N(t)$ was considered and sub-divided into mutually exclusive sub-populations of

S susceptible: healthy people not yet exposed to TB,
E latently infected: exposed to TB but not infectious,
I diagnosed infectious: have active TB confirmed after a sputum examination in a hospital,
J undiagnosed infectious: have not yet been to a hospital for diagnosis but are active for confirmation by a sputum examination,
L lost sight: people who have been diagnosed as having active TB, begun their treatment and quitted before the end,
R recovered: people cured after treatment in the hospital.

In some countries, reliable TB tests are often missing or too expensive [31]. Hence, TB diagnosis based on a single sputum examination can often only be classified as "probable" or "presumed", and cannot detect cases of less infectious forms of TB [50]. Therefore, the model is based on the following assumptions, established from behaviors of people in different epidemiological classes.

1. *Mtb transmission from diagnosed infectious to susceptible population, due to education on the infection is limited. It was therefore modeled using a standard incidence or frequency-dependent force of infection.*
2. *Mtb transmission from undiagnosed infectious to susceptible population, due to their level of education on the disease was modeled by a density-dependent force of infection.*