Journal of the Egyptian Mathematical Society (2014) 22, 311–316

Egyptian Mathematical Society
Journal of the Egyptian Mathematical Society
www.etms-eg.org
www.elsevier.com/locate/joems

ORIGINAL ARTICLE

Mathematical model on pulmonary and multidrug-resistant tuberculosis patients with vaccination

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Received 11 May 2013; accepted 22 July 2013
Available online 5 September 2013

KEYWORDS
Pulmonary tuberculosis;
Multidrug-resistant tuberculosis;
Vaccination;
Epidemic model;
Stability

Abstract Tuberculosis is a global epidemic disease and almost two billion people across the globe are infected with the tuberculosis bacilli. Many countries like China, Europe and United States has achieved dramatic decrease in TB mortality rate but country like India is still struggling hard to control this epidemic. Jharkhand one of the states of India is highly epidemic toward this disease. We propose a mathematical model to understand the spread of tuberculosis disease in human population for both pulmonary and drug-resistant subjects. A number of new vaccines are currently in development. Keeping in mind, vaccination as one of the treatment for TB patients may be infant or adult in future; an assumption for the transfer of proportion of susceptible population to the vaccination class is considered. Quarantine class is also considered in our epidemic model for multidrug-resistant patients, and it is observed that it may play a vital role for controlling the disease. Threshold and equilibria are obtained and the condition for epidemic under different conditions of threshold is established. Real parametric values of the Jharkhand state are taken into account to simulate the system developed, and the results so obtained validate our analytical results.

2000 MATHEMATICS SUBJECT CLASSIFICATION: 92D30; 34D23; 93D20

1. Introduction

TB is among the most ancient diseases. German Microbiologist Robert Koch discovered the causative organism *Mycobacterium tuberculosis* on 24th March 1882. From Forties to seventies of 20th century, different anti-Tuberculosis drugs came into existence. World Health Organization (WHO) declared TB as global epidemic in 1993. Tuberculosis (TB) has been around for centuries and today it infects one-third of the world population. While tuberculosis has been stamped out in the developed world, it remains a serious and constant threat to the lives of people in resource-poor countries, killing almost two million people a year. Tuberculosis is a contagious disease that spreads like the common cold. Active tuberculosis develops primarily in people with weakened immune systems, especially in people with HIV, and can trigger a serious

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Peer review under responsibility of Egyptian Mathematical Society.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.joems.2013.07.006

infection to the lungs, resulting in death. 4400 people die of tuberculosis every day for a total of nearly two million deaths a year [1]. 30% of the world population—two billion people—are infected with the tuberculosis bacilli; one in ten of these people will become sick with active tuberculosis and without effective treatment; it will infect 10–15 other people in a year [1]. Tuberculosis prevention and control face serious challenges, but Global Fund programs are helping countries around the world to fight back.

Global Fund programs are up and running throughout the world, playing a leadership role in stopping the spread of tuberculosis. Worldwide, Global Fund programs have treated 7.7 million tuberculosis cases with DOTS therapy (directly observed therapy, short-course), treated 43,000 people for multi-drug-resistant tuberculosis (MDR-TB), provided tuberculosis and HIV co-infection services to 2.4 million, and trained 12.2 million health or community workers [1]. Roughly, a third of the world population has been infected with *M. tuberculosis*, and new infections occur at a rate of one per second. However, not all infections with *M. tuberculosis* cause tuberculosis disease and many infections are asymptomatic. In 2007, there were an estimated 13.7 million chronic active cases, and in 2010, there were 8.8 million new cases, and 1.45 million deaths, mostly in developing countries [1]. 0.35 million of these deaths occur in those co-infected with HIV. Tuberculosis is the second most common cause of death from infectious disease (after HIV). The absolute number of tuberculosis cases has been decreasing since 2005 and new cases since 2002. China has achieved particularly dramatic progress, with an 80% decline in its TB mortality rate. The distribution of tuberculosis is not uniform across the globe; about 80% of the population in many Asian and African countries tested positive in tuberculin tests, while only 5–10% of the U.S. population tested positive. India has the largest total incidence, with an estimated 2.0 million new cases. In developed countries, tuberculosis is less common and is mainly an urban disease. In the United Kingdom, the national average was 15 per 100,000 in 2007, and the highest incidence rates in Western Europe were 30 per 100,000 in Portugal and Spain. These rates compared with 98 per 100,000 in China and 48 per 100,000 in Brazil. In the United States, the overall tuberculosis case rate was 4 per 100,000 persons in 2007. In Canada, tuberculosis is still endemic in some rural areas. TB continues to be the leading killer disease for Indian adults among all infectious diseases. One-fifth of the world's TB incident cases are in India. More than 80% of TB patients have pulmonary TB. In developing countries, more than 75% of TB patients are in the economically productive age group of 15–45 years.

Children in the first five years of their life are likely to suffer from serious and fatal forms of TB, more so, if not vaccinated with BCG. Globally, it is estimated that about 1.1 million new cases are reported and 1,30,000 deaths occur annually due to TB among children. Reliable data on incidence and prevalence of the disease is not available due to difficulties in the diagnosis of pediatric TB under field conditions. However, limited data available reveal that prevalence of TB among children in the age group 0–14 years is estimated to be 0.3% of radiological cases and 0.15% of bacteriological cases. One specimen positive out of the two is enough to declare a patient as smear-positive TB. Smear-positive TB is further classified as a new or re-treatment case based on their previous treatment history, and an appropriate therapy is prescribed. Patients in whom both specimens are smear-negative should be prescribed symptomatic treatment and broad-spectrum antibiotics. Spread of TB Disease in the state of Jharkhand (India) in the year 2010–2011is given in Table 1 [2].

The journey so far in the development of mathematical TB propagation has been studied using the epidemiological modeling [3–6] in which the disease status are divided into different compartments which is initiated by Kermack and McKendrick [7] and later extended by Baile [8], Anderson and May [9]. The SIS (Susceptible-Infected-Susceptible) and SIR (Susceptible-Infected-Recovered) models are highly applicable and suggested model, and SIR model assumes that once a host recovers from the disease, it becomes immune forever while the SIS model has been used for diseases where repeat infections are common. The SEIR model proposed by Yan and Liu [10] assumes that the recovered hosts have a permanent immunization period with a certain probability, which is not consistent with real situation. In [4], the authors used epidemiologic data on tuberculosis to construct a model for the time delay from initial latent infection to active disease, when infection transmission occurs. They used case rate tables in the United States to calculate the fractional rate of change per annum (A) in the incidence of active tuberculosis. They then derived estimates for the effective reproductive number (R) and the cumulative transmission, defined as the number of people whom one infected person will infect in his or her lifetime and over many multiple successive transmissions, respectively. Smith and Cheeseman [5] discussed a model to compare the efficacy of various disease control strategies, including temporary and permanent sterilization. By using rabies and TB as examples of acute and chronic diseases, the model shows that lethal control can be more effective at disease eradication in an isolated population than vaccination. This is due to the birth of larger numbers of susceptible individuals during a vaccination campaign, which makes it harder to keep the population below the critical threshold density. This difference was very marked for the progressive disease of tuberculosis. Gammaitoni and Nucci [6] evaluated the efficacy of recommended tuberculosis (TB) infection control measures by using a deterministic mathematical model for airborne contagion. They examined the percentage of purified protein derivative conversions under various exposure conditions, environmental control strategies, and respiratory protective devices. They concluded that environmental control cannot eliminate the risk for TB transmission during high-risk procedures; respiratory protective devices, and particularly high-efficiency particulate air masks, may provide nearly complete protection if used with air filtration or ultraviolet irradiation.

2. Epidemic model

We propose susceptible-exposed-infectious-quarantine-recovered-susceptible with vaccination compartment (SEIQRS-V) model to describe the dynamics of TB propagation with respect to time in human population. We assume constant birth rate in the population, which may die naturally at a constant rate. Initially, we assume the population to be susceptible toward TB infection. Before a subject become fully infectious, he/she shows the symptom of TB disease like having cough with mild fever; such subjects are put into *exposed* compartment (E). Subjects which are having pulmonary TB are put into the infectious compartment (I) and are subjected to six