BERKELEY PUBLICATION

09.30.2019 AND RESEARCH INTERNATIONAL

Journal of Med., Biological and Pharm. Sci. Vol. 10 No. 3

DYNAMIC ANALYSIS USING AN SEIR EPIDEMIC MODEL WITH DEMOGRAPHY FOR EXPOSE AND INFECTIVE; TUBERCULOSIS DISEASE IN BALI LOCAL GOVERNMENT AREA OF TARABA STATE.

MUKHTAR SUNUSI HASSAN & [2]USMAN ABDULLAHI SANI

**General Studies Department School of General Studies and Management Technology, Federal Polytechnic Bali, P. M. B 05 Bali, Taraba State **Statistics Department, School of Science and Technology, Federal Polytechnic Bali, P. M. B 05 Bali. Taraba State.*

ABSTRACT

A SEIR model for the transmission of an infectious disease (tuberculosis) that spreads in a population through direct contact of the hosts is studied. The force of infection is of proportionate Mixing type. A threshold R_0 which determines the outcome of the disease; if $R_0 < 1$, the infected fraction of the population disappears so the disease dies out, while if $R_0 > 1$, the infected fraction persists and a unique endemic equilibrium state is shown, under a mild restriction on the parameters, to be globally asymptotically stable in the interior of the feasible region, case study (Bali, LGA Taraba State). Two other threshold parameters $\boldsymbol{\delta}$ and $\boldsymbol{\sigma}$ are also identified; they determine the dynamics of the population sizes in the cases when the disease dies out and when it is endemic, respectively.

Introduction:

Tuberculosis has been present in humans since decade. The earliest unambiguous detection of M. tuberculosis involves evidence of the disease in the remains of bison in Wyoming dated to around 1000 years ago. Then it was transferred to humans, and diverged from a common ancestor, is currently unclear. A comparison of the genes of M. tuberculosis complex (MTBC) in humans to MTBC in animals suggests humans did not acquire MTBC from animals during animal domestication, as was

ISSN: 1211-4401

Vol. 10, No. 3

Journal of Journal of Medical, Biological and Pharmaceutical Science

Keywords: *Tuberculosis, Epidemic models; Endemic equilibrium; Latent period; Global stability; compartment and Compound matrices; Basic Reproduction Numbered* R_0

Area of study: *Mathematical Modelling*

previously believed. The pulmonary form associated with tubercles was established as pathology by Dr Richard Morton in 1689, due to the variety of its symptoms, TB was not identified as a single disease until the 1820s. It was not named "tuberculosis" until 1839, by J. L. Schönlein. The scientist who contributed to discovery and solution of the disease, include:Albert Calmette, Camille Guérin Dr Richard Morton and J. L. Schönlein.

Tuberculosis caused the most widespread public concern in the 19th and early 20th centuries as an endemic disease of the urban poor, especially in European and Scandinavian countries in 1815. Also In 2017, world health organization stated that 87% of new TB cases occurred in the 30 high TB burden countries. Eight countries accounted for two thirds of the new TB cases: Nigeria, Bangladesh, South Africa and others. Improvements in public health began significantly reducing rates of tuberculosis even before the arrival of streptomycin and other antibiotics, although the disease remained a significant threat to public health such that when the Medical Research Council was formed in Britain in 1913, its initial focus was tuberculosis research.

Tuberculosis, MTB, or TB (short for tubercle bacillus), is a widespread, infectious disease caused by various strains of mycobacteria, usually Mycobacterium tuberculosis. Tuberculosis generally affects the lungs, but can also affect other parts of the body. It is spread through the air when people who have an active TB infection cough, sneeze, or otherwise transmit respiratory fluids through the air. Most infections do not have symptoms, known as latent tuberculosis. About one in ten latent infections eventually progresses to active disease which, if left untreated, kills more than 50% of those so infected. The classic symptoms of active TB infection are a chronic cough with tinged sputum, fever, night sweats, and weight loss. Infection of other organs causes a wide

range of symptoms. Diagnosis of active TB relies on radiology (commonly chest X-rays), as well as microscopic examination and microbiological culture of body fluids. Diagnosis of latent TB relies on the tuberculin skin test (TST) and/or blood tests. Treatment is difficult and requires administration of multiple antibiotics over a long period of time. Household, workplace, and social contacts are also screened and treated if necessary. Antibiotic resistance is a growing problem in multiple drug-resistant tuberculosis (MDR-TB) infections. Prevention relies on early detection and treatment of cases and on screening programs and vaccination with the bacillus Calmette-Guérin vaccine.

The rate of tuberculosis in different areas varies across the globe; about 80% of the population in many Asian and African countries tests positive in tuberculin tests, while only 5–10% of the United States population tests positive. Many people in the developing world contract tuberculosis because of a poor immune system, largely due to high rates of HIV infection and the corresponding development of AIDS

Signs and symptoms

The main symptoms of variants and stages of tuberculosis are given, with many symptoms overlapping with other variants, while others are more (but not entirely) specific for certain variants. Multiple variants may be present simultaneously. Tuberculosis may infect any part of the body, but most commonly occurs in the lungs (known as pulmonary tuberculosis). The signs and symptoms include fever, chills, night sweats, loss of appetite, weight loss, and fatigue. Significant nail clubbing may also occur.

Causes

According to the medical scientists stated that the main cause of Tuberculosis (TB) is Mycobacterium tuberculosis, a small, aerobic, non motile bacillus. The high lipid content of this pathogen accounts for many of its unique clinical characteristics. It divides every 16 to 20 hours, which is an extremely slow rate compared with other bacteria, which usually divide in less than an hour. Mycobacteria have an outer membrane lipid bilayer. In nature, the bacterium can grow only within the cells of a host

organism, but M. tuberculosis can be cultured in the laboratory.

Risk factors

A number of factors make people more susceptible to TB infections. According to World health organisation (WHO) report in 2013 that the most important risk factor globally is HIV; 13% of all people with TB are infected by the virus. This is a particular problem in sub-Saharan Africa, where rates of HIV are high. Of people without HIV who are infected with tuberculosis, about 5–10% develop active disease during their lifetimes; in contrast, 30% of those co infected with HIV develop the active disease. Tuberculosis is closely linked to both overcrowding and malnutrition, making it one of the principal diseases of poverty. Those at high risk thus include: people who inject illicit drugs, inhabitants and employees of locales where vulnerable people gather (e.g. prisons and homeless shelters), medically under privileged and resource-poor communities, high-risk ethnic minorities, children in close contact with high-risk category patients, and health-care providers serving these patients. Chronic lung disease is another significant risk factor. Those who smoke cigarettes have nearly twice the risk of TB compared to non smokers.

Transmission

When people with active pulmonary TB cough, sneeze, speak, sing, or spit, they expel infectious aerosol droplets 0.5 to 5.0 μm in diameter. A single sneeze can release up to 40,000 droplets. Each one of these droplets may transmit the disease, since the infectious dose of tuberculosis is very small (the inhalation of fewer than 10 bacteria may cause an infection).

People with prolonged, frequent, or close contact with people with TB are at particularly high risk of becoming infected, with an estimated 22% infection rate. A person with active but untreated tuberculosis may infect 10–15 (or more) other people per year. Transmission should occur from only people with active TB – those with latent infection are not thought to be contagious. The probability of transmission from one person to another depends upon several factors, including the number of infectious droplets expelled by the

carrier, the effectiveness of ventilation, the duration of exposure, the virulence of the M. Tuberculosis strain, the level of immunity in the uninfected person, and others. The cascade of person-to-person spread can be circumvented by effectively segregating those with active ("overt") TB and putting them on anti-TB drug regimens. After about two weeks of effective treatment, subjects with non resistant active infections generally do not remain contagious to others. If someone does become infected, it typically takes three to four weeks before the newly infected person becomes infectious enough to transmit the disease to others.

Pathogenesis

About 90% of those infected with M. tuberculosis have asymptomatic, latent TB infections (sometimes called LTBI), with only a 10% lifetime chance that the latent infection will progress to overt, active tuberculosis disease. In those with HIV, the risk of developing active TB increases to nearly 10% a year. If effective treatment is not given, the death rate for active TB cases is up to 66%. TB infection begins when the mycobacteria reach the pulmonary alveoli, where they invade and replicate within endosomes of alveolar macrophages. Macrophages identify the bacterium as foreign and attempt to eliminate it by phagocytosis..

WHO 2013, state that tuberculosis is classified as one of the granulomatous inflammatory diseases. Macrophages, T lymphocytes, B lymphocytes, and fibroblasts aggregate to form granulomas, with lymphocytes surrounding the infected macrophages. When other macrophages attack the infected macrophage, they fuse together to form a giant multinucleated cell in the alveolar lumen. The granuloma may prevent dissemination of the mycobacteria and provide a local environment for interaction of cells of the immune system.

Diagnosis

Diagnosing active tuberculosis based merely on signs and symptoms is difficult, as is diagnosing the disease in those who are immune suppressed. A diagnosis of TB should, be considered in those with signs of lung disease

or constitutional symptoms lasting longer than two weeks. A chest X-ray and multiple sputum cultures for acid-fast bacilli are typically part of the initial evaluation. Interferon-γ release assays and tuberculin skin tests are of little use in the developing world.

A definitive diagnosis of TB is made by identifying M. tuberculosis in a clinical sample (e.g., sputum, pus, or a tissuebiopsy). However, the difficult culture process for this slow-growing organism can take two to six weeks for blood or sputum culture. Thus, treatment is often begun before cultures are confirmed.

Prevention

Tuberculosis prevention and control efforts primarily rely on the vaccination of infants and the detection and appropriate treatment of active cases. The World Health Organization has achieved some success with improved treatment regimens, and a small decrease in case numbers.

Vaccines

Tuberculosis vaccines and BCG vaccine

The laboratory scientists' state only available vaccine as of 2011 is Bacillus Calmette-Guérin (BCG). In children it decreases the risk of getting the infection by 20% and the risk of infection turning into disease by nearly 60%.It is the most widely used vaccine worldwide, with more than 90% of all children being vaccinated. The immunity it induces decreases after about ten years. As tuberculosis is uncommon in most of states of federation, BCG is administered to only those people at high risk. Part of the reasoning arguing against the use of the vaccine is that it makes the tuberculin skin test falsely positive, so is of no use in screening. A number of new vaccines are currently in development.

Management

Treatment of TB uses antibiotics to kill the bacteria. Effective TB treatment is difficult, due to the unusual structure and chemical composition of the mycobacterial cell wall, which hinders the entry of drugs and makes many antibiotics ineffective. The two antibiotics most commonly used are

isoniazid and rifampicin, and treatments can be prolonged, taking several months. Latent TB treatment usually employs a single antibiotic, while active TB disease is best treated with combinations of several antibiotics to reduce the risk of the bacteria developing antibiotic resistance. People with latent infections are also treated to prevent them from progressing to active TB disease later in life. Directly observed therapy, is recommended by the WHO in an effort to reduce the number of people not appropriately taking antibiotics. The evidence to support this practice over people simply taking their medications independently is poor. Methods to remind people of the importance of treatment do, however, appear effective.

Prognosis

Age-standardizeddisability-adjusted life years caused by tuberculosis per 100,000 inhabitants in 2008.

no data	75–100	750–1000
≤10	100–250	1000–2000
10–25	250–500	2000–3000
25–50	500–750	≥ 3000
50–75		

Progression from TB infection to overt TB disease occurs when the bacilli overcome the immune system defences and begin to multiply. In primary TB disease (some 1–5% of cases), this occurs soon after the initial infection. However, in the majority of cases, a latent infection occurs with no obvious symptoms. These dormant bacilli produce active tuberculosis in 5–10% of these latent cases, often many years after infection.

Epidemiology

Epidemiology of tuberculosis

In 2007, the prevalence of TB per 100,000 people was highest in sub-Saharan Africa, and was also relatively high in Asia.

Roughly one-third of the world's population has been infected with M. tuberculosis, with new infections occurring in about 1% of the population each year. However, most infections with M. tuberculosis do not cause TB disease,] and 90–95% of infections remain asymptomatic. In 2012, an

estimated 8.6 million chronic cases were active. In 2010, 8.8 million new cases of TB were diagnosed, and 1.20–1.45 million deaths occurred, most of these occurring in developing countries. Of these 1.45 million deaths, about 0.35 million occur in those also infected with HIV.

Tuberculosis is the second-most common cause of death from infectious disease (after those due to HIV/AIDS). The total number of tuberculosis cases has been decreasing since 2005, while new cases have decreased since 2002. China has achieved particularly dramatic progress, with about an 80% reduction in its TB mortality rate between 1990 and 2010. The number of new cases has declined by 17% between 2004–2014.Tuberculosis is more common in developing countries; about 80% of the population in many Asian and African countries test positive in tuberculin tests, while only 5–10% of the US population test positive. Hopes of totally controlling the disease have been dramatically dampened because of a number of factors, including the difficulty of developing an effective vaccine, the expensive and time-consuming diagnostic process, the necessity of many months of treatment, the increase in HIV-associated tuberculosis, and the emergence of drug-resistant cases in the 1980s.

In 2007, the country with the highest estimated incidence rate of TB was Swaziland, with 1,200 cases per 100,000 people. India had the largest total incidence, with an estimated 2.0 million new cases. In developed countries, tuberculosis is less common and is found mainly in urban areas. Rates per 100,000 people in different areas of the world were: globally 178, Africa 332, the Americas 36, Eastern Mediterranean 173, Europe 63, Southeast Asia 278, and Western Pacific 139 in 2010. In Canada and Australia, tuberculosis is many times more common among the aboriginal peoples, especially in remote areas. In the United States Native Americans have a fivefold greater mortality from TB, and racial and ethnic minorities accounted for 84% of all reported TB cases.

The rate of TB varies with age. In Africa, it primarily affects adolescents and young adults. However, in countries where incidence rates have declined dramatically (such as the United States), TB is mainly a disease of older people and the immune compromised (risk factors are listed above).

Worldwide, 22 "high-burden" states or countries together experience 80% of cases as well as 83% of deaths.

Society and culture

Public health efforts

The World Health Organization, Bill and Melinda Gates Foundation, and US government are subsidizing a fast-acting diagnostic tuberculosis test for use in low- and middle-income countries. In addition to being fast-acting, the test can determine if there is resistance to the antibiotic rifampicin which may indicate multi-drug resistant tuberculosis and is accurate in those who are also infected with HIV. Many resource-poor places as of 2011 only have access to sputum microscopy.

India had the highest total number of TB cases worldwide in 2010, in part due to poor disease management within the private and public health care sector. Programs such as the Revised National Tuberculosis Control Program are working to reduce TB levels amongst people receiving public health care.

A 2014 the EIU-healthcare report that the need to address apathy and urging for increased funding. The report cites among others Lucica Ditui "[TB] is like an orphan. It has been neglected even in countries with a high burden and often forgotten by donors and those investing in health interventions."

Slow progress has led to frustration, expressed by executive director of the Global Fund to Fight AIDS, Tuberculosis and Malaria – Mark Dybul: "we have the tools to end TB as a pandemic and public health threat on the planet, but we are not doing it." Several international organizations are pushing for more transparency in treatment, and more countries are implementing mandatory reporting of cases to the government, although adherence is often sketchy. Commercial treatment-providers may at times overprescribe second-line drugs as well as supplementary treatment, promoting demands for further regulations. The government of Brazil provides universal TB-care, which reduces this problem. Conversely falling rates of TB-infection may not relate to the number of programs directed at reducing infection rates, but may be tied to increased level of education,

income and health of the population. Costs of the disease, as calculated by the World Bank in 2009 may exceed 150 billion USD per year in "high burden" countries. Lack of progress eradicating the disease may also be due to lack of patient follow-up – as among the 250M rural migrants in China.

Research

The BCG vaccine has limitations, and research to develop new TB vaccines is ongoing, a number of potential candidates are currently in phase I and II clinical trials. Two main approaches are being used to attempt to improve the efficacy of available vaccines. One approach involves adding a subunit vaccine to BCG, while the other strategy is attempting to create new and better live vaccines. MVA85A, an example of a subunit vaccine, currently in trials in South Africa, is based on a genetically modified vaccinia virus. Vaccines are hoped to play a significant role in treatment of both latent and active disease.

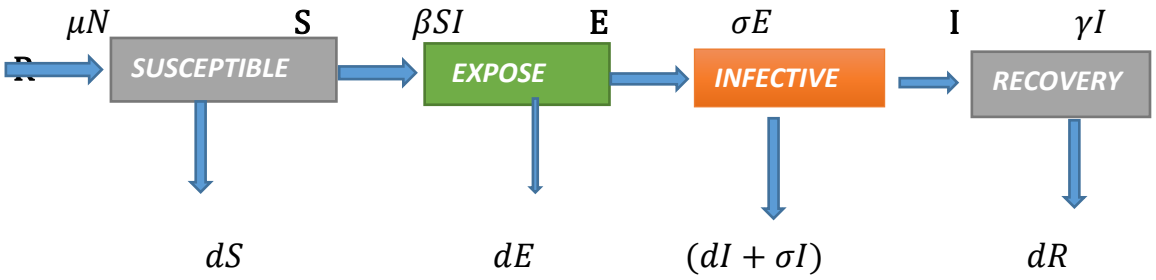
To encourage further discovery, researchers and policymakers are promoting new economic models of vaccine development, including prizes, tax incentives, and advance market commitments. A number of groups, including the Stop TB Partnership, the Nigerian Tuberculosis Vaccine Initiative, and the Aeras Global TB Vaccine Foundation, are involved with research. A number of medications are being studied for multi drug resistant tuberculosis including: bedaquiline and delamanid. Bedaquiline received U.S. Food and Drug Administration (FDA) approval in late 2012. The safety and effectiveness of these new agents are still uncertain, because they are based on the results of a relatively small studies. However, existing data suggest that patients taking bedaquiline in addition to standard TB therapy are five times more likely to die than those without the new drug, which has resulted in medical journal articles raising health policy questions about why the FDA approved the drug and whether financial ties to the company making bedaquiline influenced physicians' support for its use.

Materials and methods

Mathematical model (The SEIR model)

For many important infections there is a significant incubation period during which the individual has been infected but is not yet infectious

themselves. During this period the individual is in compartment E (for exposed).



- S is the fraction of susceptible individuals (those able to contract the disease),
- E is the fraction of exposed individuals (those who have been infected but are not yet infectious),
- I is the fraction of infective individuals (those capable of transmitting the disease),
- R is the fraction of recovered individuals (those who have become immune).

Note that the variables give the *fraction* of individuals - that is, we have normalized them so that

Further more the parameters: $\beta, \sigma, \gamma, \sigma, \varepsilon_o, \frac{A}{\mu}$ are all positive constants, α is a non-negative constant. , suppose that:

- μ =There are equal birth and death rates,
- $\frac{1}{\sigma}$ = the mean latent period for the disease,
- $\frac{1}{\gamma}$ = the mean infectious period,
- recovered individuals are permanently immune, so there is no transfer from the R class back to the S class
- β = the contact rate may be a function of time.
- γ = the rate constant for recovery
- ε_o = the rate constant at which the exposed individuals become infective.
- $\frac{1}{\varepsilon_o}$ = the mean latent period.

- $\frac{A}{\mu}$ = represents a carrying capacity, or maximum possible population size.

This leads us to consider the following model:

$$\frac{dS}{dt} = \mu - \beta SI - \mu S \ldots\ldots\ldots 1$$

$$\frac{dE}{dt} = \beta SI - \sigma E - \mu E \ldots\ldots\ldots 2$$

$$\frac{dI}{dt} = \sigma E - \gamma I - \mu I \ldots\ldots\ldots\ldots 3$$

$$\frac{dR}{dt} = \gamma I - \mu R \ldots\ldots\ldots\ldots\ldots\ldots 4$$

From the above equation, $\frac{dN}{dt} = 0$ and N = S+E+I+R thus constant.

The model assumes that recovered individual is immune from infection for life. Therefore in the absence of vaccination, the basic Reproduction ratio $R_O = \frac{\sigma}{\sigma+\mu}\frac{\beta}{\gamma+\mu} = \frac{\sigma\beta}{(\sigma+\mu)(\gamma+\mu)}$

it can be shown that for $R_O > 1$ the model has a fixed point with I = 0 which is unstable, and a fixed point with I > 0, which M stable, etc.

We know consider steady - state of model:

$$S^* = \frac{(\sigma+\mu)(\gamma+\mu)}{\sigma\beta},\ E^* = \frac{\mu(\gamma+\mu)R_O - 1}{\sigma\beta},\ I^* = \frac{\mu(R_O-1)}{\sigma\beta}$$

$$R = 1 - S^* - E^* - I^*$$

Therefore $(S^*, E^*, I^*) = \left\{\frac{(\sigma+\mu)(\gamma+\mu)}{\sigma\beta}, \frac{\mu(\gamma+\mu)R_O-1}{\sigma\beta}, \frac{\mu(R_O-1)}{\sigma\beta}\right\}$, $R_O = \frac{\beta\alpha}{((\sigma+\mu)(\gamma+\mu))}$

Similarly to the SIR model, also in this case we have a Disease-Free-Equilibrium (steady - state), (N,0,0,0) and an Endemic Equilibrium EE, and one can show that, independently form biologically meaningful initial conditions it holds that:

$(S(O), E(O), I(O), R(O)) \in \{(S,E,I,R): [S \geq 0, E \geq 0, I \geq 0, R \geq 0]$, $[S + E + I + R]$

$$R_O \leq 1 \Longrightarrow \lim_{n\to\infty}(S(t), E(t), I(t), R(t)) = \text{DFE} = (\text{N}, 0, 0, 0)$$

$$R_O > 1, \text{I(O)} > 0 \Longrightarrow \lim_{t\to\infty}(S(t), E(t), I(t), R(t)) = \text{EE}$$

In case of periodically varying contact rate $\beta(t)$ the condition for the global attractiveness of DFE is that the following linear system with periodic coefficients:

$$\frac{dE_1}{dt} = \beta(t)I_1 - (\gamma + \alpha)E_1$$
$$\frac{dI_1}{dt} = \alpha E_1(t) - (\gamma + \mu)I_1$$

is stable (i.e. it has its Floquet's eigenvalues inside the unit circle in the complex plane). Therefore the disease free equilibrium or state $P_o = \left\{0, 0, 0, \frac{A}{\mu}\right\}$ and R_o is the numbered of secondary infection caused by a newly typical infected individual entering the population at the disease-free equilibrium (steady - state) during his or her entire infectious period, so R_o is called the basic reproduction number. Then from the steady state we established globally asymptotic of seir equation for $P_o = \left\{0, 0, 0, \frac{A}{\mu}\right\}$ is stable if $R_o \leq 1$, and unstable if $R_o > 1$.

Using Jacobian matrix n $\times$ n of P_o is

$$A = \begin{bmatrix} \frac{df_1}{du_1} & \frac{df_1}{du_2} & \frac{df_1}{du_3} & \frac{df_1}{du_4} \\ \frac{df_2}{du_1} & \frac{df_2}{du_2} & \frac{df_2}{du_3} & \frac{df_2}{du_4} \\ \frac{df_3}{du_1} & \frac{df_3}{du_2} & \frac{df_3}{du_3} & \frac{df_3}{du_4} \\ \frac{df_4}{du_1} & \frac{df_4}{du_2} & \frac{df_4}{du_3} & \frac{df_4}{du_4} \end{bmatrix}_{(u^*_1, u^*_2 u^*_3, u^*_4)} \qquad |A - \lambda I| = \begin{bmatrix} -\omega & \frac{\alpha A}{\mu h(\frac{A}{\mu})} & 0 & 0 \\ \varepsilon & -\delta & 0 & 0 \\ 0 & \gamma & -1 & 0 \\ 0 & -\alpha & 0 & -1 \end{bmatrix}$$

and because there is only one non-zero element in the third column and in the fourth column, respectively, and they are both negative, we may reduce the question of whether the eigen-values of this matrix have negative real part to the same question for the 2 $\times$2 matrix

$$\mathrm{J} = \begin{bmatrix} -\omega & \frac{\alpha A}{\mu h(\frac{A}{\mu})} \\ \varepsilon & -\delta \end{bmatrix}_{2\times 2}$$

The trace of jacobian is clearly negative, and the condition that the determinant of J is R0 < 1. Thus the disease-steady state (free equilibrium) is unstable if R0 > 1.

If R0 > 1, the endemic equilibrium P^* of the system of SEIR equation is locally asymptotically stable. Then The matrix of the linearization of the system equation in non dimensionalization at the equilibrium $P^* = \{E^*, I^*, R^*, N^*\}$,

Then the jacobian matrix after rigorous substitution is going to be in the form

$$|A - \lambda I| = \begin{bmatrix} -\omega - \frac{\alpha I^*}{hN^*} & \frac{\delta\omega}{\varepsilon} - \frac{\alpha I^*}{hN^*} & \frac{-\alpha I^*}{hN^*} & \rho^* \\ \varepsilon & -\delta & 0 & 0 \\ 0 & \gamma & -1 & 0 \\ 0 & -\alpha & 0 & -1 \end{bmatrix}$$

then the characteristic equation of the jacobian is $(\lambda + 1)(\lambda^3 + a_1\lambda^2 + a_2) = 0$, where the value a_1, a_2. are determine further explanation, therefore the endemic equilibrium P^* of which exists if R0 > 1, is always locally asymptotically stable.

Conclusions and discussion

The research has considered a SEIR model that incorporates recruitment and exponential natural death, as well as disease-related death, so that the total population size may vary in time. distinguishing feature of the SEIR model considered here is that tuberculosis is a disease that has significant impact on human being from ancient period to present date, where significant and scientific achievement has been upon the solution of its drugs, intensive campaign and awareness against the disease, and strong contribution from both the government, private organization and individuals for eradication of tuberculosis in the whole world, The basic reproduction number R0 defined by (2.5) of this SEIR model (2.2) is a sharp threshold parameter which completely determines the global dynamics of the system (2.2) and the outcome of the disease. If $R_O \leq 1$, the disease-free equilibrium is globally stable so that the disease always

dies out, and if $R_O > 1$, the disease-free equilibrium becomes unstable while the endemic equilibrium emerges as the unique positive equilibrium and it is globally stable in the interior of the feasible region, (Bali LGA of Taraba State). In the special case when the mean latent period $\frac{1}{\varepsilon_o} \to 0$ or the mean infective period $\frac{1}{\gamma} \to \infty 1$, the SEIR model here reduces to an SIR model or an SEIR model with recruitment and saturating contact rate respectively. Thus, the global dynamic results of these two models can be obtained as special cases when $\frac{1}{\varepsilon_o} = 0$ and $\gamma - 0$ respectively. Especially, to prove the global stability of the endemic equilibrium, we make a change of variable by which our four dimensional model can be reduced to a three-dimensional asymptotical autonomous system with limit system.

Then the Euler method gives the following sequence of approximations:

$$t_{n+1} = t_n + h$$
$$S_{n+1} = S_n + h(\mu - \beta S_n I_n - \mu S_n)$$
$$E_{n+1} = E_n + h(\beta S_n I_n - \sigma E_n - \mu E_n)$$
$$I_{n+1} = I_n + h(\sigma E_n - \gamma I_n - \mu I_n)$$
$$R_{n+1} = R_n + h(\gamma I_n - \mu R_n)$$

Also the Basic Reproduction Numbered $R_O = \frac{\beta\alpha}{((\sigma+\mu)(\gamma+\mu))}$

I program this sequence into Excel with giving Initial values and parameter values

Initial values: $S(o) = 0.90, E(o) = 0.06, I(o) = 0.04, R(o) = 0$

Parameter values: $h = 0.4$, $\beta = 95$ per year, then $\beta = \frac{95}{365} = 0.2587$ per days, $\frac{1}{\mu} = 3$ years, $\Longrightarrow \mu = \frac{1}{3\times365} = 0.0001108$, $\frac{1}{\sigma} = 3$ years, $\Longrightarrow \sigma = \frac{1}{1\times365} = 0.968987$

The graph of SEIR Model with demography

		Beta	0.2587	mu	0.001108	sigma	0.96899	gamma	0.14286
		h	0.4						
S/N	tn	Sn	En	In	Rn	Ro	CHECK		
1	0	0.9	0.06	0.04	0	0.0372	1		

2	0.4	0.89591	0.04044	0.060952	0.002286		0.99959		
3	0.8	0.88964	0.0304	0.073118	0.005768		0.99893		
4	1.2	0.88213	0.02534	0.08069	0.009943		0.9981		
5	1.6	0.87383	0.02287	0.085863	0.01455		0.99711		
6	2	0.865	0.02176	0.089783	0.01945		0.99599		
7	2.4	0.85577	0.02135	0.093047	0.024572		0.99474		
8	2.8	0.8462	0.02131	0.095965	0.029878		0.99335		
9	3.2	0.83634	0.02144	0.098697	0.035348		0.99183		
10	3.6	0.8262	0.02166	0.101324	0.040972		0.99016		
11	4	0.81579	0.02192	0.103886	0.046744		0.98834		
12	4.4	0.80513	0.02218	0.106399	0.05266		0.98637		
13	4.8	0.7942	0.02244	0.108871	0.058716		0.98423		
14	5.2	0.78303	0.02268	0.111299	0.064911		0.98192		
15	5.6	0.77161	0.0229	0.11368	0.071243		0.97943		
16	6	0.75994	0.02309	0.116009	0.077707		0.97675		
17	6.4	0.74804	0.02325	0.118278	0.084302		0.97388		
18	6.8	0.73592	0.02339	0.120479	0.091023		0.9708		
19	7.2	0.72357	0.02349	0.122605	0.097867		0.96753		
20	7.6	0.711	0.02355	0.124648	0.10483		0.96403		
21	8	0.69823	0.02358	0.126599	0.111906		0.96032		
22	8.4	0.68527	0.02358	0.12845	0.119091		0.95639		
23	8.8	0.67211	0.02354	0.130192	0.126378		0.95222		
24	9.2	0.65879	0.02346	0.131818	0.133761		0.94782		
25	9.6	0.6453	0.02334	0.13332	0.141235		0.94319		
26	10	0.63166	0.02319	0.13469	0.14879		0.93833		
27	10.4	0.61788	0.02299	0.135921	0.156421		0.93322		
28	10.8	0.60399	0.02276	0.137006	0.164119		0.92787		
29	11.2	0.58999	0.02249	0.137939	0.171875		0.92229		
30	11.6	0.57589	0.02219	0.138713	0.179681		0.91647		
31	12	0.56173	0.02184	0.139325	0.187528		0.91042		
32	12.4	0.5475	0.02147	0.139768	0.195406		0.90414		
33	12.8	0.53324	0.02105	0.140039	0.203306		0.89764		
34	13.2	0.51896	0.02061	0.140136	0.211218		0.89092		
35	13.6	0.50467	0.02014	0.140055	0.219132		0.884		
36	14	0.4904	0.01964	0.139796	0.227038		0.87687		
37	14.4	0.47616	0.01911	0.139357	0.234926		0.86955		
38	14.8	0.46197	0.01856	0.13874	0.242785		0.86205		

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39	15.2	0.44785	0.01799	0.137945	0.250606		0.85439		
40	15.6	0.43382	0.0174	0.136975	0.258377		0.84657		
41	16	0.4199	0.0168	0.135833	0.26609		0.83862		
42	16.4	0.4061	0.01618	0.134522	0.273734		0.83053		
43	16.8	0.39244	0.01556	0.133048	0.281299		0.82234		
44	17.2	0.37894	0.01492	0.131415	0.288777		0.81406		
45	17.6	0.36562	0.01429	0.129632	0.296159		0.80569		
46	18	0.35248	0.01365	0.127704	0.303435		0.79727		
47	18.4	0.33956	0.01301	0.125639	0.310598		0.7888		
48	18.8	0.32685	0.01238	0.123446	0.31764		0.78031		
49	19.2	0.31437	0.01175	0.121134	0.324553		0.77181		
50	19.6	0.30214	0.01113	0.118712	0.331331		0.76331		
51	20	0.29017	0.01052	0.11619	0.337968		0.75485		
52	20.4	0.27846	0.00993	0.113578	0.344457		0.74642		
53	20.8	0.26702	0.00935	0.110886	0.350795		0.73805		
54	21.2	0.25587	0.00878	0.108124	0.356976		0.72976		
55	21.6	0.24502	0.00824	0.105302	0.362996		0.72155		
56	22	0.23445	0.00771	0.102432	0.368852		0.71345		
57	22.4	0.22419	0.0072	0.099522	0.374542		0.70546		
58	22.8	0.21424	0.00672	0.096583	0.380063		0.6976		
59	23.2	0.20459	0.00625	0.093625	0.385414		0.68988		
60	23.6	0.19526	0.00581	0.090657	0.390593		0.68231		
61	24	0.18623	0.00539	0.087688	0.3956		0.67491		
62	24.4	0.17752	0.00499	0.084726	0.400435		0.66767		
63	24.8	0.16912	0.00461	0.081779	0.405099		0.6606		
64	25.2	0.16102	0.00425	0.078856	0.409593		0.65372		
65	25.6	0.15323	0.00392	0.075962	0.413917		0.64703		
66	26	0.14575	0.0036	0.073106	0.418075		0.64053		
67	26.4	0.13856	0.00331	0.070291	0.422067		0.63423		
68	26.8	0.13167	0.00303	0.067525	0.425896		0.62812		
69	27.2	0.12507	0.00277	0.064811	0.429566		0.62222		
70	27.6	0.11875	0.00254	0.062154	0.433079		0.61652		
71	28	0.11271	0.00232	0.059559	0.436439		0.61102		
72	28.4	0.10694	0.00211	0.057027	0.439649		0.60572		
73	28.8	0.10143	0.00192	0.054561	0.442713		0.60063		
74	29.2	0.09618	0.00175	0.052165	0.445634		0.59573		
75	29.6	0.09119	0.00159	0.049839	0.448418		0.59103		

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76	30	0.08643	0.00144	0.047585	0.451067		0.58653		
77	30.4	0.08191	0.00131	0.045405	0.453586		0.58221		
78	30.8	0.07762	0.00119	0.043297	0.45598		0.57808		
79	31.2	0.07355	0.00107	0.041264	0.458252		0.57414		
80	31.6	0.06969	0.00097	0.039303	0.460407		0.57037		
81	32	0.06604	0.00088	0.037416	0.462448		0.56678		
82	32.4	0.06258	0.00079	0.035602	0.464382		0.56335		
83	32.8	0.05931	0.00072	0.033859	0.46621		0.56009		
84	33.2	0.05622	0.00065	0.032187	0.467938		0.55699		
85	33.6	0.05331	0.00058	0.030583	0.46957		0.55405		
86	34	0.05056	0.00053	0.029048	0.47111		0.55125		
87	34.4	0.04798	0.00047	0.027579	0.472561		0.54859		
88	34.8	0.04555	0.00043	0.026174	0.473927		0.54608		
89	35.2	0.04326	0.00038	0.024832	0.475213		0.54369		
90	35.6	0.04112	0.00035	0.023551	0.476421		0.54144		
91	36	0.0391	0.00031	0.022329	0.477556		0.5393		
92	36.4	0.03722	0.00028	0.021164	0.47862		0.53729		
93	36.8	0.03546	0.00025	0.020055	0.479617		0.53538		
94	37.2	0.03381	0.00023	0.018998	0.480551		0.53359		
95	37.6	0.03227	0.00021	0.017993	0.481423		0.53189		
96	38	0.03084	0.00019	0.017037	0.482238		0.5303		
97	38.4	0.0295	0.00017	0.016128	0.482998		0.5288		
98	38.8	0.02827	0.00015	0.015265	0.483706		0.52739		
99	39.2	0.02712	0.00014	0.014445	0.484363		0.52606		
100	39.6	0.02605	0.00012	0.013666	0.484974		0.52482		
101	40	0.02507	0.00011	0.012928	0.48554		0.52365		
102	40.4	0.02416	0.0001	0.012227	0.486064		0.52256		
103	40.8	0.02333	9.4E-05	0.011563	0.486547		0.52154		
104	41.2	0.02257	8.5E-05	0.010933	0.486992		0.52058		
105	41.6	0.02187	7.8E-05	0.010337	0.487401		0.51969		
106	42	0.02123	7.1E-05	0.009771	0.487776		0.51885		
107	42.4	0.02066	6.5E-05	0.009236	0.488118		0.51808		
108	42.8	0.02014	5.9E-05	0.00873	0.488429		0.51735		
109	43.2	0.01967	5.5E-05	0.00825	0.488712		0.51668		
110	43.6	0.01925	5E-05	0.007796	0.488966		0.51606		
111	44	0.01887	4.6E-05	0.007366	0.489195		0.51548		
112	44.4	0.01855	4.3E-05	0.00696	0.489399		0.51495		

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113	44.8	0.01826	3.9E-05	0.006576	0.48958		0.51446		
114	45.2	0.01802	3.7E-05	0.006213	0.489739		0.514		
115	45.6	0.01781	3.4E-05	0.005869	0.489877		0.51359		
116	46	0.01764	3.2E-05	0.005544	0.489995		0.51321		
117	46.4	0.0175	2.9E-05	0.005237	0.490095		0.51286		
118	46.8	0.01739	2.8E-05	0.004947	0.490177		0.51254		
119	47.2	0.01732	2.6E-05	0.004673	0.490242		0.51226		
120	47.6	0.01727	2.4E-05	0.004414	0.490292		0.512		
121	48	0.01725	2.3E-05	0.004169	0.490327		0.51177		
122	48.4	0.01725	2.1E-05	0.003938	0.490348		0.51156		
123	48.8	0.01728	2E-05	0.003719	0.490356		0.51137		
124	49.2	0.01733	1.9E-05	0.003513	0.490351		0.51121		
125	49.6	0.0174	1.8E-05	0.003318	0.490334		0.51107		
126	50	0.01749	1.7E-05	0.003134	0.490306		0.51095		
127	50.4	0.0176	1.6E-05	0.00296	0.490268		0.51085		
128	50.8	0.01773	1.5E-05	0.002795	0.49022		0.51076		
129	51.2	0.01788	1.4E-05	0.00264	0.490162		0.5107		
130	51.6	0.01804	1.4E-05	0.002494	0.490096		0.51065		
131	52	0.01822	1.3E-05	0.002356	0.490021		0.51061		
132	52.4	0.01841	1.2E-05	0.002225	0.489939		0.51059		
133	52.8	0.01862	1.2E-05	0.002102	0.489849		0.51058		
134	53.2	0.01883	1.1E-05	0.001985	0.489752		0.51058		
135	53.6	0.01906	1.1E-05	0.001875	0.489648		0.5106		
136	54	0.0193	1E-05	0.001772	0.489538		0.51062		
137	54.4	0.01955	9.8E-06	0.001673	0.489423		0.51066		
138	54.8	0.01982	9.4E-06	0.001581	0.489301		0.51071		
139	55.2	0.02009	9E-06	0.001494	0.489175		0.51076		
140	55.6	0.02037	8.6E-06	0.001411	0.489043		0.51083		
141	56	0.02065	8.2E-06	0.001333	0.488907		0.5109		
142	56.4	0.02095	7.9E-06	0.00126	0.488767		0.51098		
143	56.8	0.02125	7.6E-06	0.00119	0.488622		0.51107		
144	57.2	0.02156	7.2E-06	0.001124	0.488474		0.51117		
145	57.6	0.02188	6.9E-06	0.001063	0.488321		0.51127		
146	58	0.02221	6.7E-06	0.001004	0.488166		0.51138		
147	58.4	0.02254	6.4E-06	0.000949	0.488007		0.5115		
148	58.8	0.02287	6.1E-06	0.000897	0.487845		0.51162		
149	59.2	0.02321	5.9E-06	0.000847	0.48768		0.51174		

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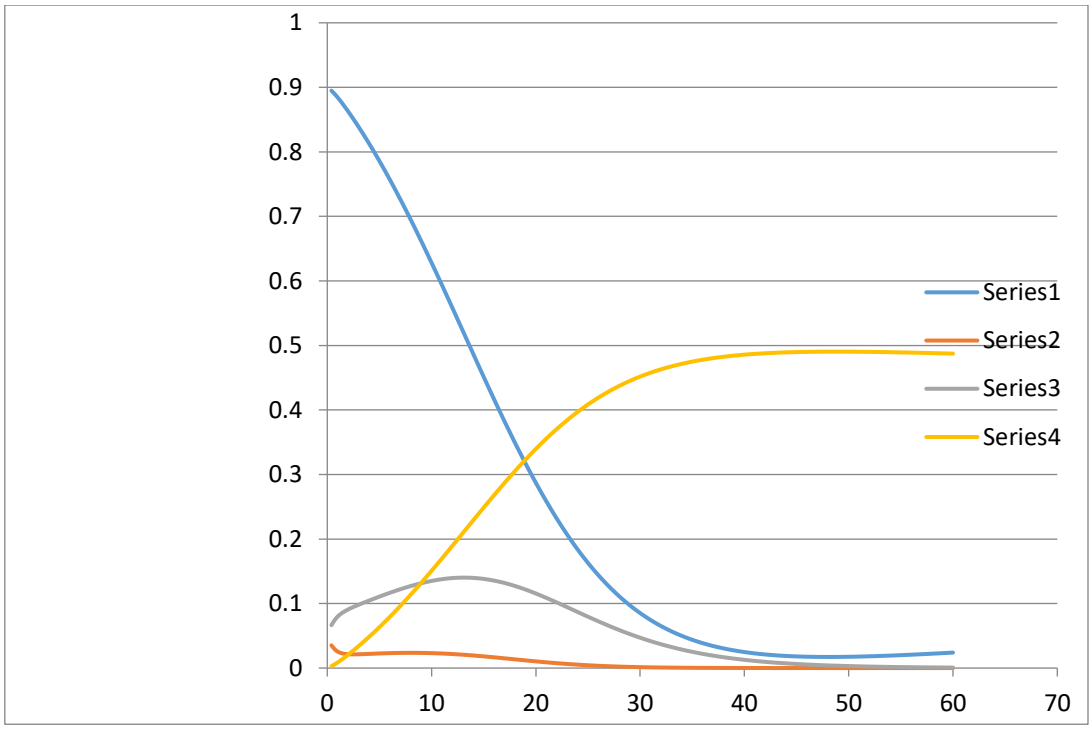
150	59.6	0.02356	5.6E-06	0.000801	0.487512		0.51187		
151	60	0.02391	5.4E-06	0.000757	0.487342		0.51201		

Analysis and interpretation of graph

From the computation of the data it shown that due to various majors taken by the government, nongovernmental organization, public and private individual reduces drastically impact of tuberculosis worldwide. Also public awareness/campaign against tuberculosis, research on drugs & vaccine and taken appropriate measures give significant effect on tuberculosis nationwide From the graph the basic reproduction number, $R_O = \frac{\beta\alpha}{((\sigma+\mu)(\gamma+\mu))} < 1$ which shows that disease dies out and stable at steady- state..

The vaccine effectiveness is also taken into account. We investigate the global dynamics of the reduced proportional system. If $R_O \leq 1$, the disease-free equilibrium P_o is globally asymptotically stable.



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