ON THE NUMERICAL SIMULATIONS OF A MATHEMATICAL MODEL OF TUBERCULOSIS WITH EFFECT OF IMMUNIZATION AND INFECTIOUS TUBERCULOSIS TREATMENT

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Absract
In this study we used Euler's numerical method to derive an algorithm for the solution of an existing mathematical model for preventing mother to child transmission of tuberculosis using Bacillus Calmette-Guerin. The algorithm was used to produce a software for simulation using visual basic programming language. We observed that total eradication of Tuberculosis within two decades is only achievable when there is at least 90 % immunization coverage along side with very low contraction rate.

Keywords: Mathematical Model, Tuberculosis, Immunization and Total Eradication

Introduction

In 1993, concerned with the rising cases of deaths and infection rates, the World Health Organization (WHO) declared tuberculosis as a global emergency. Approximately a third of the worlds' population wass affected by tuberculosis, particularly affecting people in developing countries where 99% of tuberculosis deaths occur. Of the 1.7 billion people estimated to be infected with tuberculosis, 1.3 billion live in developing countries.

Despite many decades of study, the widespread availability of vaccines, an arsenal of anti-microbial drugs and, more recently, a highly visible World Health Organization effort to promote a unified global control strategy, tuberculosis (TB) remains a leading cause of infectious mortality. It is responsible for approximately two million deaths each year. Although TB is currently well-controlled in most countries, recent data indicate 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 (Dye, 2006). In these regions, the emergence of drug-resistant TB and the convergence of the HIV (human immunodeficiency virus) and TB epidemics have created substantial new challenges for disease control.

Bacillus Calmette-Guérin (or Bacille Calmette-Guérin, BCG) is a vaccine against tuberculosis that is prepared from a strain of the attenuated (weakened) live bovine tuberculosis bacillus, *Mycobacterium bovis*, that has lost its virulence in humans by being specially cultured in an artificial medium for years. The bacilli have retained enough strong antigenicity to become a somewhat effective vaccine for the prevention of human tuberculosis. At best, the BCG vaccine is 80% effective in preventing tuberculosis for a duration of 15 years; however, its protective effect appears to vary according to geography Colditz et al (1994).

Mathematical models can be defined as the process of creating a mathematical representation of some phenomena in order to gain a better understanding of then. It is therefore, an abstraction of reality in to the world of mathematics. Any phenomena which have the ability to grow or decay over time can be represented by a mathematical model and then solved analytically where feasible or in several cases tools of advanced calculus and Functional analysis are employed to study and interpret the dynamics. Sowumi (1993) described this as experimenting on paper which is safer than using human or animal lives. Also, numerical or computer simulations of such models can be carried out. The analysis of such models will then give an insight into the dynamics of the real life situation. Mathematical knowledge such as the existence of equilibrium

states and their stability analysis are of great interest in the mathematical models of population dynamics.

Mathematical models have played great role in discussing the dynamics of Tuberculosis, this includes Okyere (2007) who proposed a deterministic compartmental models of HIV and TB, but this model did not take into account that latently infected individual can recover without progressing to infectious class, He also stated that Successfully treated Infectious individuals move back to slow rate Latent class this is not also realistic, this happens when re infection occurs else they move into recovered class.

Yusuf (2008) also proposed a deterministic compartmental model but ignored the different rates of progression from latent to infectious class, this however precludes the speedy progression of TB caused by HIV infections. By weakening the immune system of a TB patient, HIV acts as catalyst in the progression of TB from latent class to infectious class. A patient with AIDS who become infected with mycobacterium tuberculosis has a 50% chance of developing active tuberculosis within 2 months and a 5 to 10% chance of developing active disease there after, infants and young children are also more likely to develop active TB than older people since their immune system are not yet well developed (WHO report 2003)

Hughes et al (2006) established that progression to active TB is said to be rapid if it occurs within 5 years after infection. The same paper also stated that 14% of HIV negative people or early HIV positive people develop active TB within these five years after which the progression is slow which is 0.001/year. Also 67% of people who are in their late stage of HIV develop TB within 5 years, after that the progression is slow, 0.1/year Hughes et al (2006).

Enagi, (2011), Enagi and Ibrahim (2011a), Enagi and Ibrahim (2011b) and Enagi, (2013) presented four new deterministic compartmental mathematical models for the dynamics of tuberculosis taking into consideration the effect of HIV/AIDS on immune system and administration of BCG vaccines as immunity against infection.

In this work we extended the work of Enagi and Ibrahim (2011b) by developing a software for numerical simulation of the model in order to have a clear insight into the dynamics of the model.

Materials and Method

The Model as presented in Enagi and Ibrahim (2011b) was described by a system of four differential equations as shown below.

$$\frac{dM}{dt} = \theta\rho - (\alpha + \mu)M \qquad (1)$$

$$\frac{dS}{dt} = (1-\theta)\rho + \alpha M - \beta SI - \mu S \qquad (2)$$

$$\frac{dI}{dt} = \beta SI - (\gamma + \mu + \delta)I \qquad (3)$$

$$\frac{dR}{dt} = \gamma I - \mu R \qquad (4)$$

The model parameters and variables are given below with their respective descriptions

M(t) :- Immuned compartment at time t.

S(t) :- Susceptible compartment at time t.

R(t):- Recovered compartment at time

I (t):- Infectious compartment at time t.

ρ :- Recruitment rate.
μ :- Natural death rate.
α :- Removal rate from Immuned compartment into Susceptible compartment at time t.
β :- Tuberculosis instantaneous incidence rate per Susceptible.
θ :- Proportion of the Susceptible class Immunized at birth against Infection .
δ :- Tuberculosis induced death rate
γ - Recovery rate of I(t).

Numerical Solution

The system of equations in the model was converted into difference equations using Euler's numerical method (Stroud and Dexter, 2003).

$$f(a+h) = f(a) + hf'(a)$$

Where *h* is the step size and $f'(a)$ is the derivative of $f(a)$.

From (1)

$$M'(t) = \theta\rho - (\alpha + \mu)M(t)$$

Thus, by the Euler's method:

$$M(t+h) = M(t) + hM'(t)$$

We have that

$$M(t+h) = M(t) + h[\theta\rho - (\alpha + \mu)M(t)]$$

With *h=1,* we have

$$M(t+1) = M(t) + \theta\rho - (\alpha + \mu)M(t)$$

Similarly from (2)

$$S'(t) = (1-\theta)\rho + \alpha M(t) - \beta S(t)I(t) - \mu S(t)$$

And hence the Euler's method with *h=1* leads to

$$S(t+1) = S(t) + (1-\theta)\rho + \alpha M(t) - \beta S(t)I(t) - \mu S(t)$$

From (3)

$$I'(t) = \beta S(t)I(t) - (\gamma + \mu + \delta)I(t)$$

So that Euler's method with *h=1* gives

$$I(t+1) = I(t) + \beta S(t)I(t) - (\gamma + \mu + \delta)I(t)$$

From (4)

$$R'(t) = \gamma I(t) - \mu R(t)$$

Consequently , Euler's method also gives

$$R(t+1) = R(t) + \gamma I(t) - \mu R(t)$$

The resulting difference equations was coded using visual basic programming language to produce the software for the simulations (Appendix A).

Results and Discussion

Numerical Simulations of the Model

This section presents graphs generated using the model-based software developed with visual basic programming language. The aim of this is to study the profile of the population in respect of the distinct compartments in the model and to consider the effect of varying some parameter values on the population.

From the available literature, we adopted the following values for the parameters in the model

Recruitment rate ρ = 0.045 (National Population Commission, Abuja, 2008).
Natural death rate μ= 0.014 (National Population Commission, Abuja, 2008).
Movement rate from Latent class to infectious class τ = 0.03 (Sanchez and Blower 1997, WHO 2006a, WHO 2006b).
Recovery rate of I(t) γ =0.23 (National Tuberculosis And Leprosy Control Programme Abuja, 2008).
Tuberculosis induced death rate δ = 0.001 (Estimated from National (Tuberculosis And Leprosy Control Programme Abuja, 2008))
Expiration of vaccine efficacy α (varied hypothetically).
Tuberculosis contraction rate β (varied hypothetically).

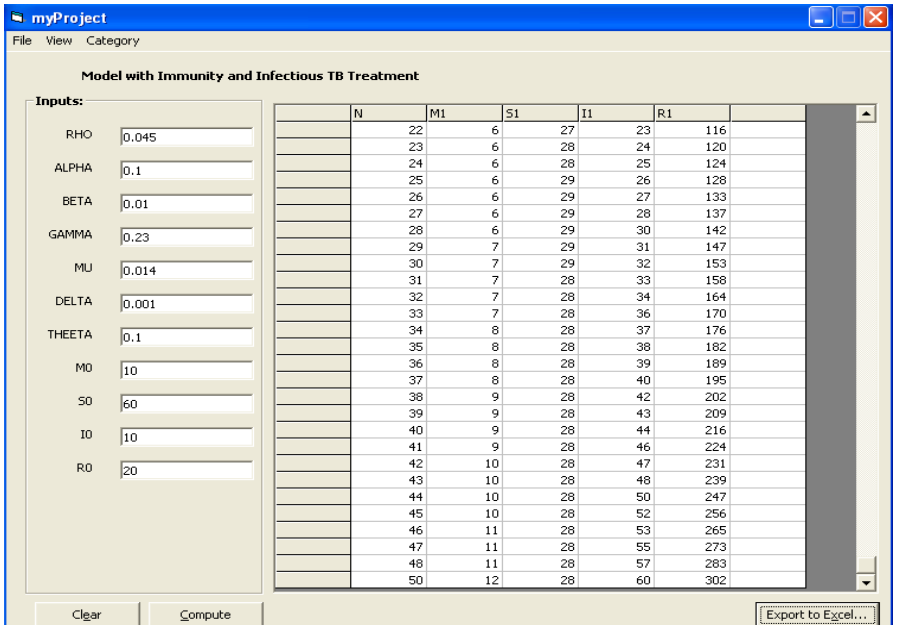

Figure 1: Software interface

The following graphs were obtained for the model with the initial conditions of M(0) = 10, S(0) = 60, I(0) = 10 and R(0) = 20.

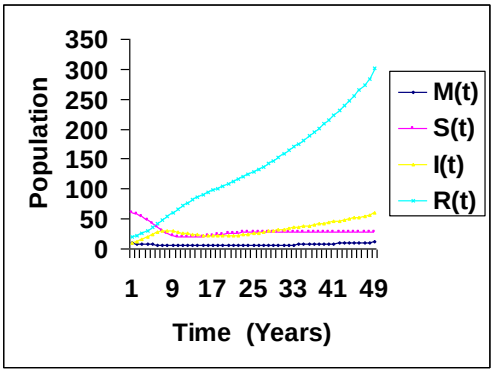

Fig 2: Graphical profile of the compartments for $\alpha = 0.1, \beta = 0.01 \& \theta = 0.1$

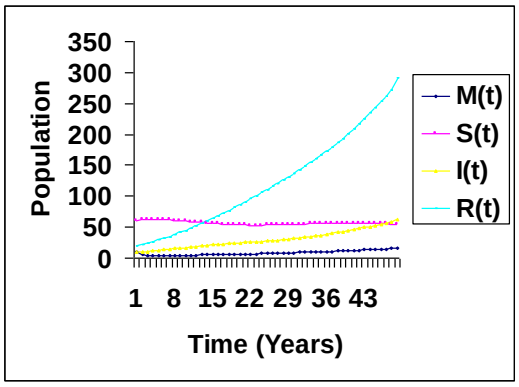

Fig 3 Graphical profile of the compartments for $\alpha = 0.5, \beta = 0.005 \& \theta = 0.5$

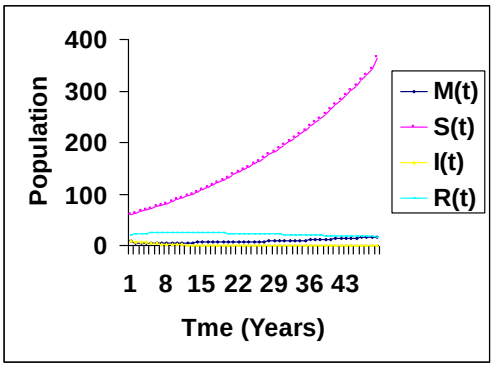

Fig 4: Graphical profile of the compartments for $\alpha = 0.9, \beta = 0.001 \& \theta = 0.9$

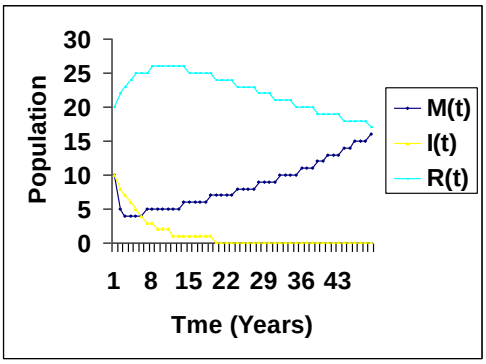

Fig 5: Closer view of M(t), I(t) and R(t) for $\alpha = 0.9, \beta = 0.001 \& \theta = 0.9$

Fig 2 shows the graphical profile of each compartment in the model for $\alpha = 0.1, \beta = 0.01 \& \theta = 0.1$ implying High contraction rate and low immunisation coverage. It was observed that R(t) was increasing rapidly. The susceptible compartment was gradually decreasing from the beginning until the 11th year. From the 11th to the 28th year, the Susceptible and Infectious classes were fluctuating until the 30th year when the two compartments continue to increase gradually leading to a TB endemic state.

With 50% immunization coverage and subsequent reduction in contraction rate 0.005 as shown in fig 3, it took the susceptible class 24 years to decrease gradually from 60 to 53 and then continue to increase gradually until the 48th year when it began to decrease again compared to fig 2 where the susceptible class decreased to as low as 20 within 14 years. The Infectious class increased steadily and intercepts with the susceptible class after 47 years when the susceptible class began to decrease while the infectious class continued increasing. This happened as early as 27th year in fig 2.

Increasing both α and θ to 0.9 and reducing β to 0.001 (i.e. low contraction rate and High immunisation coverage) as shown in figure 4, brought down the number of infectious individuals to 1 at t=12 and complete eradication at t=20. The immuned class was increasing steadily from t=20 at the same rate of decrement of R(t); this is because there was no more infectious individuals to be treated.

Conclusion

In order to achieve complete eradication of Tuberculosis within two decades there must be at least 90% immunization coverage along side with very low contraction rate. Introduction of

Latent TB treatment into this model will guarantee total eradication of Tuberculosis earlier than this time. The result of this study agrees with Enagi and Ibrahim, (2011b)

Recommendations

Efforts should be intensified to move the nation out of the current endemic situation to a stable disease free nation. This can be achieved by committing more effort and resources into

(i) detecting and treating Latently infected individuals;
(ii) reducing the break down of immune system of HIV patients by procurement of Antiretroviral drugs;
(iii) immediate isolation and commencement of treatment of Infectious TB cases;
(iv) administering Tuberculin Skin Test to all contacts to an infectious TB case;
(v) isoniazid preventive therapy should be administered to those positive to Tuberculin Skin Test.

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Appendix A

Source code for the software

```
'/**************************************************************************
'//  File Name: frmMain.frm
'//  File Size: 33.9 KB
'//  File Date: 7/9/13  10:14:32 AM
'// Printed On: Fri. July 9, 2013  10:15:31 AM
'/**************************************************************************

'Option Explicit
Dim i, x       As Integer
Attribute x.VB_VarUserMemId = 1073938432

Private Sub Form_Load()
   N = GetSetting(App.Title, "Settings", "N", N)
   A = GetSetting(App.Title, "Settings", "A", A)
   ClearTextBoxes

   Me.MSFlxGrd_TT.Clear
   Me.MSFlxGrd_TT.Rows = 50
   Me.MSFlxGrd_TT.Cols = 7

End Sub

Private Sub cmdExport_Click()
'Define the required variable
   Dim Data_Row As Integer, Data_Col As Integer

   Dim Excel  As Excel.Application        ' This is the excel program
   Dim ExcelWBk As Excel.Workbook         ' This is the work book
   Dim ExcelWS As Excel.Worksheet         ' This is the sheet

   If Not Excel Is Nothing Then Set Excel = Nothing
   Set Excel = CreateObject("Excel.Application")        'Create Excel Object.
```

```
   Set ExcelWBk = Excel.Workbooks.Add        'Add this Workbook to Excel.
   Set ExcelWS = ExcelWBk.Worksheets(1)        ' Add this sheet to this Workbook
   'Fill the Excel Sheet
   For Data_Row = 0 To Me.MSFlxGrd_TT.Rows - 1
      For Data_Col = 0 To Me.MSFlxGrd_TT.Cols - 1        '***MODIFIED***
         'For Data_Col = 1 To Me.MSFlxGrd_TT.Cols - 1    '**PREVIOUOSLY**
         Me.MSFlxGrd_TT.Row = Data_Row
         Me.MSFlxGrd_TT.Col = Data_Col
         ExcelWS.Cells(Data_Row + 1, Data_Col + 1) = Me.MSFlxGrd_TT.Text
      Next
   Next
   Me.CommonDialog1.ShowSave
   If        Len(Me.CommonDialog1.FileName)        >        0        Then        ExcelWBk.SaveAs
Me.CommonDialog1.FileName
   ' Close the WorkBook
   ExcelWBk.Close
   ' Quit Excel app
   Excel.Quit
   Set Excel = Nothing
End Sub

Private Sub cmdNew_Click()
'clear textboxes
   ClearTextBoxes
   ClearListView
End Sub

Private Sub mnuData_Click()
   InitialiseVariables
End Sub

Private Sub cmdCompute_Click()
   On Error Resume Next

      RHO = Val(Text(0).Text)
      AP = Val(Text(1).Text)
      BT = Val(Text(2).Text)
      GM = Val(Text(3).Text)
      MU = Val(Text(4).Text)
      DT = Val(Text(5).Text)
      TT = Val(Text(6).Text)
      M = Val(Text(7).Text)
      S = Val(Text(8).Text)
      i = Val(Text(9).Text)
      R = Val(Text(10).Text)

      For K = 1 To N

         Me.MSFlxGrd_TT.Row = K
         Me.MSFlxGrd_TT.Col = 1
         Me.MSFlxGrd_TT.Text = K

         Me.MSFlxGrd_TT.Row = K
         Me.MSFlxGrd_TT.Col = 2
```

```
        Me.MSFlxGrd_TT.Text = Format(M, "0")

        Me.MSFlxGrd_TT.Row = K
        Me.MSFlxGrd_TT.Col = 3
        Me.MSFlxGrd_TT.Text = Format(S, "0")

        Me.MSFlxGrd_TT.Row = K
        Me.MSFlxGrd_TT.Col = 4
        Me.MSFlxGrd_TT.Text = Format(i, "0")

        Me.MSFlxGrd_TT.Row = K
        Me.MSFlxGrd_TT.Col = 5
        Me.MSFlxGrd_TT.Text = Format(R, "0")

        T = S + L + i + R
        RH = RHO * T
        M = M + TT * RH - (AP + MU) * M
        S = S + (1 - TT) * RH + AP * M - BT * S * i - MU * S
        i = i + BT * S * i - (GM + MU + DT) * i
        R = R + GM * i - MU * R

    Next K

End Sub

Sub
   ClearLabels
   lblModelType.Caption = "Model With Immunity and Infectious TB Treatment"
   Me.Label(0).Caption = "RHO"
   Me.Label(1).Caption = "ALPHA"
   Me.Label(2).Caption = "BETA"
   Me.Label(3).Caption = "GAMMA"
   Me.Label(4).Caption = "MU"
   Me.Label(5).Caption = "DELTA"
   Me.Label(6).Caption = "THEETA"
   Me.Label(7).Caption = "M0"
   Me.Label(8).Caption = "S0"
   Me.Label(9).Caption = "I0"
   Me.Label(10).Caption = "R0"

   For i = 0 To 10
      Text(i).Visible = True
   Next

   Text(11).Visible = False
   Text(12).Visible = False
   Text(13).Visible = False


   Me.MSFlxGrd_TT.Row = 0
   Me.MSFlxGrd_TT.Col = 1
   Me.MSFlxGrd_TT.Text = "N"

   Me.MSFlxGrd_TT.Row = 0
   Me.MSFlxGrd_TT.Col = 2
```

```
    Me.MSFlxGrd_TT.Text = "M1"

    Me.MSFlxGrd_TT.Row = 0
    Me.MSFlxGrd_TT.Col = 3
    Me.MSFlxGrd_TT.Text = "S1"

    Me.MSFlxGrd_TT.Row = 0
    Me.MSFlxGrd_TT.Col = 4
    Me.MSFlxGrd_TT.Text = "I1"

    Me.MSFlxGrd_TT.Row = 0
    Me.MSFlxGrd_TT.Col = 5
    Me.MSFlxGrd_TT.Text = "R1"
End Sub

Private Sub mnuFileNew_Click()
    cmdNew_Click
End Sub

Private Sub mnuHelpAbout_Click()
    frmAbout.Show vbModal, Me
End Sub

Private Sub mnuN_Click()
    On Error Resume Next
    frmOptions.Show
End Sub

Private Sub mnuViewStatusBar_Click()
    mnuViewStatusBar.Checked = Not mnuViewStatusBar.Checked
    sbStatusBar.Visible = mnuViewStatusBar.Checked
End Sub

Sub ClearTextBoxes()
'clears all textboxes
    Dim i
    For i = 0 To 13
        Text(i).Text = ""
    Next
End Sub

Sub ClearLabels()
'clears all labels
    Dim i
    For i = 0 To 13
        Label(i).Caption = ""
    Next
End Sub

Sub ClearListView()
    On Error Resume Next
    Me.MSFlxGrd_TT.Clear
End Sub

Private Sub mnuFileExit_Click()
```

```
'unload the form
   Unload Me
End Sub

Private Sub Form_Unload(Cancel As Integer)
   Dim i      As Integer

   'close all Sub forms
   For i = Forms.Count - 1 To 1 Step -1
      Unload Forms(i)
   Next
   If Me.WindowState <> vbMinimized Then
      SaveSetting App.Title, "Settings", "MainLeft", Me.Left
      SaveSetting App.Title, "Settings", "MainTop", Me.Top
      SaveSetting App.Title, "Settings", "MainWidth", Me.Width
      SaveSetting App.Title, "Settings", "MainHeight", Me.Height
      SaveSetting App.Title, "Settings", "N", N
      SaveSetting App.Title, "Settings", "A", A

   End If
End Sub
```