

A MATHEMATICAL MODEL FOR ATTENUATING THE SPREAD OF DIABETES AND ITS MANAGEMENT IN A POPULATION

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ABSTRACT

We study the dynamics of diabetes in a population based on the etiology of the disease. In carrying out the study, we proposed that; a population generate non-diabetic non . susceptible sub-population, and a non-diabetic susceptible sub-population, the non-diabetic susceptible sub-population can further generate a population of diabetics without complication, who can later transit to a population with diabetic complications. Based on the etiology dynamics, we proposed control measures at the point of transition from the population to non-diabetic susceptible population, and at the point of transition from diabetes without complications to diabetes with complications. For this study, we intend to look at the control measure. In this regard, we proposed a mathematical model for the dynamics of diabetes by incorporating a control parameter h , so as to investigate how to control diabetes in a population. The result of the study suggested that; we need to control the incidence of diabetes, $I(t)$, and improve the control measure, h , for transition from diabetes without complication to diabetes with complication. Thus entailing going further in research to; Look into the dynamics of the genetics of transmission of the diabetic gene, to investigate how to reduce the spread (and hence the incidence $I(t)$) of diabetes, and to also look into the influence of the control factor h , on the dynamics of glucose metabolism, this will give an insight on how to manage diabetic patients.

KEY WORDS: Diabetes, Population, Genes, Genetics, Etiology.

INTRODUCTION

Diabetes mellitus is a recognized consequence of hereditary haemochromatosis, David *et al* (2003). Genomic wide scans for linkage have reported a number of chromosomal regions that may harbor genes involved in type II diabetes, with the most promising, replicating findings on chromosomes 1q21-q24, 2q37, 12q24 and chromosome 20; Florence *et al*; (2003). Type I diabetes develops in individuals who are genetically susceptible; Janne *et al* (2004). In genetic epidemiology, population-based disease registers are commonly used to collect incidence and/or genotype data or other risk factor information concerning affected subjects and their relatives or a whole population, Janne (2008).

The incidence and prevalence of diabetes are increasing all over the world; complications of diabetes constitute a burden for the individuals and the whole society. It is now commonly admitted that diabetes is sweeping the globe as a silent epidemic largely contributing to the growing burden of non-communicable diseases and mainly encouraged by decreasing levels of activity and increasing prevalence of obesity, Bouteyab *et al* (2004). This trend of incidence & prevalence in a population, despite medical intervention, is a case for serious concern.

Accordingly experts suggested that the dynamics of incidence & prevalence of diabetes in a population depends on;

- 1) The dynamics of the natural history of the disease in a population (Bouteyab *et al* 2004).
- 2) The dynamics of diabetes gene frequency in a population (Masatoshi Nei, 2006).

To understand and model the above dynamics, we need to know the natural history dynamics of diabetes in a population.

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Description of the Natural History Dynamics

Bouteyab *et al*, (2004) schematically described the natural history dynamics of diabetes in a population as follows;

Let μ = rate of natural death

λ = rate of developing complications,

γ = rate of recovery from complications

δ = rate of death from complications

ν = rate of developing disability

$I(t)$ = the incidence of diabetes without complications

Then, the natural history dynamics is as follows (With notations as defined above).

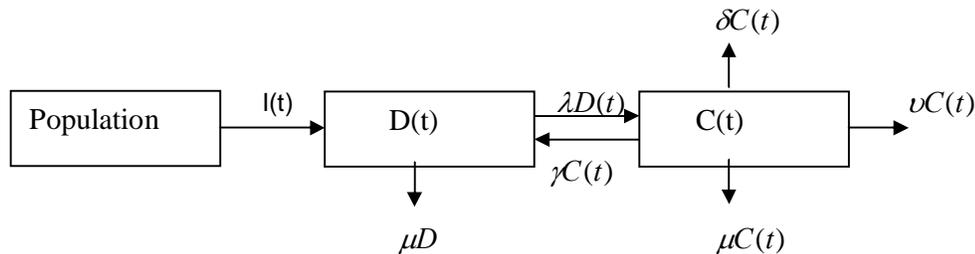


Fig. 1: Schematic model for the dynamics of diabetic population (Bouteyab *et al*)

On the basis of the above schematic model, Bouteyab *et al* (2004) developed the following mathematical model that describes the dynamics of the diabetic population;

$$\left. \begin{aligned} \frac{dC(t)}{dt} &= -(\lambda + \theta)C(t) + \lambda D(t), \quad t > 0; \quad C(0) = C_0 \\ \frac{dN(t)}{dt} &= I(t) - (\nu + \delta)C(t) - \mu N(t), \quad t > 0; \quad N(0) = N_0 \end{aligned} \right\} \text{-----(1)}$$

Where $\theta = \gamma + \mu + \nu + \delta$, $N(t) = D(t) + C(t)$

Using the above idea of the dynamics of the natural history of a diabetic population, we want to model the dynamics of diabetes in a population by incorporating control parameters, so as to investigate how to manage diabetic patients, and to regulate the spread (and thus the incidence) of diabetes in a population. For this purpose, we decomposed a population into; susceptible sub-population and Non- susceptible sub-population, and introduced control measures at two stages of the dynamics of diabetes as follows:

1. Control measure at the stage of diabetes without complication, to inhibit transition from diabetes without complication to diabetes with complication in a population
 2. Control measure at the pre susceptible stage, to reduce or inhibit the transmission of the diabetic gene, from generation to generation
- The dynamics of the subpopulations are as follows;

Susceptible Sub-population:

A member of this sub-population can;

- Move to the state of diabetic without complications (State I), and then develop (move to the state with) complications (State II) with time.

Maintaining the notations used by Bouteyab *et al* (2004) and introducing a control parameter that (supposed to) inhibits transition to diabetes with complications denoted by β , we have the following description of the dynamics.

State I: The number of diabetics without complications $D(t)$ depletes by $\mu D(t)$ & $\lambda D(t)$ as a result of natural death and transition to state of diabetes with complications respectively, and increases by $hD(t)$, $\gamma C(t)$ & $I(t)$ as a result of inhibitory control measure, recovery from complications, and incidence of diabetes without complications respectively.

State II: The number of diabetics with complications $C(t)$ depletes by $\mu C(t)$, $\nu C(t)$, $\delta C(t)$ & $\gamma C(t)$ as a result of natural death, death from complications, severe disability and recovery from complications, and increases by $\lambda D(t)$ as a result of developing complications from $D(t)$. This gives the following schematic diagram of the natural history dynamics of the diabetic sub-population.

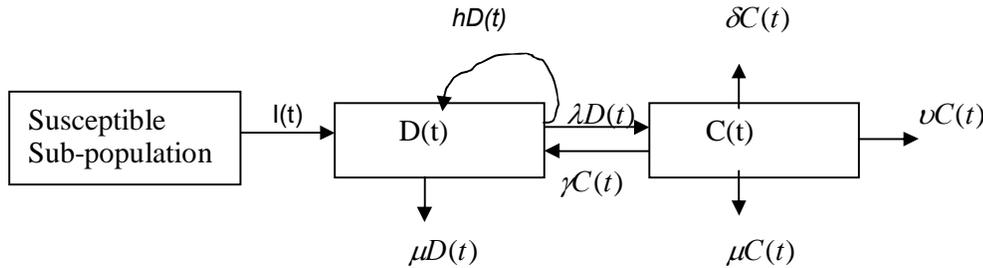


Fig. 2. Modified schematic model for the dynamics of diabetic population

Non-susceptible subpopulation:

A non susceptible person will be non-diabetic with the following dynamics

Note: Susceptible means posses the diabetic gene.

- ✓ The number of non-diabetic & non susceptible depletes as a result of natural death, and recharged from the parent population.

For this sub-population, the schematic representation of the dynamics, is as follows;



Fig. 3: Schematic model for the dynamics of non- susceptible sub-population

Fusing the two schematic models of **fig.2** & **fig.3**, and introducing diabetic gene spread inhibition parameter denoted by β , we obtained the schematic diagram of the dynamics of any given population with respect to diabetes as follows;

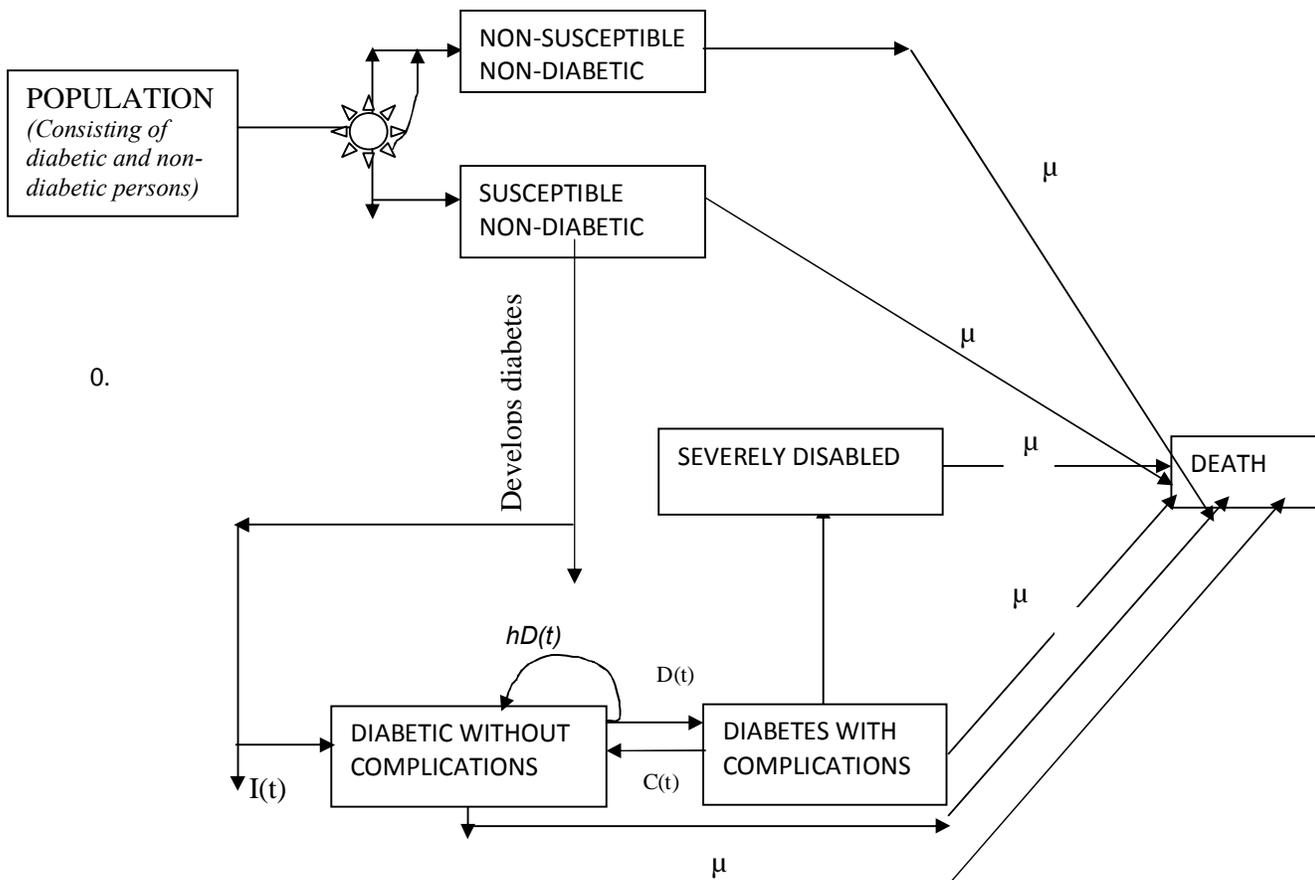


Fig. 4: Our schematic Model for the dynamics of diabetic population

In this work we are going to develop equations that describe the dynamics of diabetes in a population that incorporates the inhibitory control parameter, h , to investigate how it can play a role in retarding transition from diabetes without complications to diabetes with complications.

MODELING

Methodology

Here we state assumptions, notations, parameters, and model development

Assumptions

- ❖ Underlying population is large and finite
- ❖ Individuals are assumed to have no complications at the point of first diagnosis at any time interval from the start of the screening
- ❖ Probability () of a diabetic person developing complications is assumed to be constant.

Notations

The following notations are used;

- $I(t)$ = incidence of diabetes without complications.
- $D(t)$ = Number of diabetics without complications
- $C(t)$ = Number of diabetics with complications
- $N(t)$ = $D(t) + C(t)$ is the total population of diabetics.

Parameters:

- μ = Natural mortality rate
- d = Denotes the level of dieting in terms of calorie intake
- λ = Rate at which diabetic person develop complications
- γ = Rate at which complications are cured
- h = Rate at which transition to diabetic with complications state is inhibited,
- ν = Rate at which diabetic patients with complications becomes severely disabled.
- δ = Mortality rate due to complications.
- $\theta = \gamma + \mu + \nu + \delta$

Developing Quations

In this work, we estimate h as $h = \frac{ex}{d}$, where "ex" is the amount calories burnt as a result of physical exercise, and d is the level of dietary calorie intake.

Now, looking at the schematic diagram of the dynamics of the susceptible sub-population in **fig. 4**, the equations governing the rate of changes of $C(t)$ & $D(t)$ are as follows;

$$\left. \begin{aligned} \frac{dD(t)}{dt} &= I(t) - (\lambda - h + \mu)D(t) + \gamma C(t), & D(0) &= D_0 \\ \frac{dC(t)}{dt} &= \lambda D(t) - (\gamma + \mu + \nu + \delta)C(t), & C(0) &= C_0 = 0 \end{aligned} \right\} \text{----- (2)}$$

System (2) is the required system of equations that governs the dynamics of the susceptible sub-population depicted by the schematic diagram in fig 4.

Preliminary Result

Now looking at system (2) above, this describes

- (1) The dynamics of the diabetic population, from diabetes without complication to diabetes with complications & vice-versa in a diabetic population.

First, let us study system (2), we shall solve the system analytically so as to gain an insight into the dynamics of the evolution of the diabetic population from diabetes without complications, to diabetes with complications & vice-versa for the following reason;

Analytical solutions give room for sensitivity analysis which will give more insight into the dynamics of the diabetic population.

Assuming a steady state for $I(t)$ i. e. $I(t) = I$ (independent of time, t), and differentiating the first equation of system (2) with respect to t , we have;

$$\frac{d^2D(t)}{dt^2} = (-\lambda + h - \mu) \frac{dD(t)}{dt} + \gamma \frac{dC(t)}{dt} \text{----- (3)}$$

Using system (2) in equation (3), we have:

$$\begin{aligned} \frac{d^2D(t)}{dt^2} &= (-\lambda + h - \mu)[(-\lambda + h - \mu)D(t) + \gamma C(t) + I] + \gamma[\lambda D(t) - \theta C(t)] \\ &= (\lambda - h + \mu)^2 D(t) - (\lambda - h + \mu)\gamma C(t) - (\lambda - h + \mu)I + \gamma(\lambda D(t) - \theta C(t)) \end{aligned}$$

$$= ((\lambda - h + \mu)^2 + \gamma\lambda)D(t) - ((\lambda - h + \mu)\gamma + \gamma\theta)C(t) - (\lambda - h + \mu)I \text{ ----- (4)}$$

$$\text{Where } \theta = \gamma + \mu + \nu + \delta$$

From the first equation of system (2), we have

$$C(t) = \frac{1}{\gamma} \left(\frac{dD(t)}{dt} + (\lambda - h + \mu)D(t) - I \right) \text{ ----- (5)}$$

Using (5) in (4) we have;

$$\begin{aligned} \frac{d^2 D(t)}{dt^2} &= ((\lambda - h + \mu)^2 + \gamma\lambda)D(t) - (\gamma(\lambda - h + \mu) + \gamma\theta) \left[\frac{1}{\gamma} \left(\frac{dD(t)}{dt} + (\lambda - h + \mu)D(t) - I \right) \right] - (\lambda - h + \mu)I \\ &= ((\lambda - h + \mu)^2 + \gamma\lambda)D(t) - (\theta + \lambda - h + \mu) \frac{dD(t)}{dt} - (\lambda - h + \mu)(\theta + \lambda - h + \mu)D(t) + \\ &\quad (\theta + \lambda - h + \mu)I \quad (\lambda - h + \mu)I \\ &= -(\theta + \lambda - h + \mu) \frac{dD(t)}{dt} + \gamma\lambda D(t) - (\mu\theta - h\theta + \lambda\theta)D(t) + \theta I \\ &= -(\theta + \lambda - h + \mu) \frac{dC(t)}{dt} + (\gamma\lambda - \mu\theta + h\theta - \lambda\theta)D(t) + \theta I \end{aligned}$$

Let $\sigma = (\theta + \lambda - h + \mu)$ & $\beta = \gamma\lambda - \lambda\theta - h\theta - \theta\mu$

$$\begin{aligned} \Rightarrow \frac{d^2 D(t)}{dt^2} &= -\sigma \frac{dD(t)}{dt} + \beta D(t) + \theta I \\ &\equiv \frac{d^2 D(t)}{dt^2} + \sigma \frac{dD(t)}{dt} - \beta D(t) = \theta I \\ &\equiv \frac{d^2 D(t)}{dt^2} + \sigma \frac{dD(t)}{dt} - \beta D(t) = \theta I \text{ ----- (6)} \end{aligned}$$

The auxiliary equation for the homogeneous part of (6) is

$$m^2 + \sigma m - \beta = 0 \Rightarrow m = \frac{-\sigma \pm \sqrt{\sigma^2 + 4\beta}}{2}$$

$$\therefore D_c(t) = C_1 \exp^{\frac{1}{2}(-\sigma + \sqrt{\sigma^2 + 4\beta})t} + C_2 \exp^{\frac{1}{2}(-\sigma - \sqrt{\sigma^2 + 4\beta})t}$$

For the particular solution, we have, using method of undetermined coefficients.

$$D_p(t) = C \text{ ----- (7)}$$

Using (7) in (6), we have:

$$0 + 0 - \beta C = \theta I \Rightarrow C = -\frac{\theta I}{\beta}$$

$$\therefore D(t) = D_c(t) + D_p(t)$$

$$= C_1 \exp^{\frac{1}{2}(-\sigma + \sqrt{\sigma^2 + 4\beta})t} + C_2 \exp^{\frac{1}{2}(-\sigma - \sqrt{\sigma^2 + 4\beta})t} - \frac{(\theta I)}{\beta} \text{ ----- (8)}$$

From equation (5), we have;

$$C(t) = \frac{1}{\gamma} \left[\begin{aligned} & \frac{1}{2}(-\sigma + \sqrt{\sigma^2 + 4\beta})C_1 \exp^{\frac{1}{2}(-\sigma + \sqrt{\sigma^2 + 4\beta})t} + \frac{1}{2}(-\sigma - \sqrt{\sigma^2 + 4\beta})C_2 \exp^{\frac{1}{2}(-\sigma - \sqrt{\sigma^2 + 4\beta})t} \\ & + (\lambda - h + \mu) \left(C_1 \exp^{\frac{1}{2}(-\sigma + \sqrt{\sigma^2 + 4\beta})t} + C_2 \exp^{\frac{1}{2}(-\sigma - \sqrt{\sigma^2 + 4\beta})t} - \frac{(\theta I)}{\beta} \right) - I \end{aligned} \right]$$

$$C(t) = \frac{1}{\gamma} \left[\begin{aligned} & \left(C_1 \exp^{\frac{1}{2}(-\sigma + \sqrt{\sigma^2 + 4\beta})t} \right) \left(\frac{1}{2}(-\sigma + \sqrt{\sigma^2 + 4\beta}) + (\lambda - h + \mu) \right) \\ & + \left(C_2 \exp^{\frac{1}{2}(-\sigma - \sqrt{\sigma^2 + 4\beta})t} \right) \left(\frac{1}{2}(-\sigma - \sqrt{\sigma^2 + 4\beta}) + (\lambda - h + \mu) \right) - (\lambda - h + \mu) \left(\frac{(\theta I)}{\beta} \right) - I \end{aligned} \right] \text{Let}$$

$$\eta_1 = \frac{1}{2}(\sigma - \sqrt{\sigma^2 + 4\beta}), \eta_2 = \frac{1}{2}(\sigma + \sqrt{\sigma^2 + 4\beta})$$

$$\therefore C(t) = \frac{1}{\gamma} \left[C_1(-\eta_1 + \lambda - h + \mu) \exp(-\eta_1)t + C_2(-\eta_2 + \lambda - h + \mu) \exp(-\eta_2)t - \frac{(\lambda - h + \mu)}{\beta} (\theta I) - I \right] \text{---(9) Now}$$

(8) & (9) constitute the solution of the system (2). Using the initial conditions we have;

$$D(0) = D_0 = C_1 + C_2 - \frac{\theta I}{\beta} \text{-----(10)}$$

$$C(0) = 0 = \frac{1}{\gamma} \left(C_1(-\eta_1 + \lambda - h + \mu) + C_2(-\eta_2 + \lambda - h + \mu) - \frac{(\lambda - h + \mu)}{\beta} (\theta I) - I \right) \text{----- (11) From}$$

(10), we have;

$$C_1 = D_0 + \left(\frac{\theta I}{\beta} \right) - C_2 \text{-----(12) Using}$$

(12) in (11), we have;

$$\begin{aligned} \therefore C(0) = 0 &= \frac{1}{\gamma} \left(\left(D_0 + \left(\frac{\theta I}{\beta} \right) - C_2 \right) (-\eta_1 + \lambda - h + \mu) + C_2(-\eta_2 + \lambda - h + \mu) - \frac{(\lambda - h + \mu)}{\beta} (\theta I) - I \right) \\ &= \frac{1}{\gamma} \left(D_0(-\eta_1 + \lambda - h + \mu) - C_2(-\eta_1 + \lambda - h + \mu) + C_2(-\eta_2 + \lambda - h + \mu) + \frac{\theta I}{\beta}(-\eta_1 + \lambda - h + \mu) - \frac{(\lambda - h + \mu)}{\beta} (\theta I) - I \right) \\ &= \frac{1}{\gamma} \left(C_2(-\eta_2 + \eta_1) + D_0(-\eta_1 + \lambda - h + \mu) - \frac{(\theta I)\eta_1}{\beta} + \frac{(\theta I)}{\beta}(\lambda - h + \mu) - \frac{(\lambda - h + \mu)}{\beta} (\theta I) - I \right) \\ &= \frac{1}{\gamma} \left(C_2(-\eta_2 + \eta_1) + D_0(-\eta_1 + \lambda - h + \mu) - \frac{(\theta I)}{\beta} \eta_1 - I \right) \end{aligned}$$

$$0 = \frac{\beta C_2(-\eta_2 + \eta_1) + D_0(-\eta_1 + \lambda - h + \mu)\beta - (\theta I)\eta_1 - I\beta}{\beta}$$

$$0 = C_2(-\eta_2 + \eta_1)\beta + D_0(-\eta_1 + \lambda - h + \mu)\beta - (\theta I)\eta_1 - I\beta$$

$$\Rightarrow C_2 = \frac{-D_0(-\eta_1 + \lambda - h + \mu)\beta + (\theta I)\eta_1 + I\beta}{(-\eta_2 + \eta_1)\beta}$$

Equation (12) now becomes

$$\begin{aligned}
 C_1 &= D_0 + \frac{(\theta I)}{\beta} + \frac{D_0(-\eta_1 + \lambda - h + \mu)\beta - (\theta I)\eta_1 - I\beta}{(-\eta_2 + \eta_1)\beta} \\
 &= \frac{D_0\beta(-\eta_2 + \eta_1) + (\theta I)(-\eta_2 + \eta_1) + D_0(-\eta_1 + \lambda - h + \mu)\beta - (\theta I)\eta_1 - I\beta}{(-\eta_2 + \eta_1)\beta} \\
 &= \frac{-D_0\beta\eta_2 + D_0\beta\eta_1 - (\theta I)\eta_2 + (\theta I)\eta_1 - D_0\beta\eta_1 + D_0(\lambda - h + \mu)\beta - (\theta I)\eta_1 - I\beta}{(-\eta_2 - \eta_1)\beta} \\
 &= \frac{-D_0\beta\eta_2 - (\theta I)\eta_2 + D_0(\lambda - h + \mu)\beta - I\beta}{(-\eta_2 - \eta_1)\beta} \\
 &= \frac{D_0\beta(-\eta_2 + \lambda - h + \mu) - (\theta I)\eta_2 - I\beta}{(-\eta_2 + \eta_1)\beta}
 \end{aligned}$$

Therefore the solutions C(t) & D(t) to system (2) are:

$$D(t) = C_1 \exp(-\eta_1)t + C_2 \exp(-\eta_2)t - \frac{\theta I}{\beta} \text{----- (13)}$$

$$C(t) = \frac{1}{\gamma} \left(C_1(-\eta_1 + \lambda - h + \mu)\exp(-\eta_1)t + C_2(-\eta_2 + \lambda - h + \mu)\exp(-\eta_2)t - \frac{(\lambda - h + \mu)}{\beta}(\theta I) - I \right) \text{---- (14)}$$

where

$$\theta = \gamma + \mu + \nu + \delta$$

$$\sigma = \theta + \lambda - h + \mu$$

$$; \beta = \gamma\lambda - \lambda\theta + \theta h - \mu\theta$$

$$\eta_1 = \frac{1}{2} \left(\sigma - \sqrt{\sigma^2 + 4\beta} \right)$$

$$\eta_2 = \frac{1}{2} \left(\sigma + \sqrt{\sigma^2 + 4\beta} \right)$$

$$C_1 = \frac{D_0\beta(-\eta_2 + \lambda - h + \mu) - (\theta I)\eta_2 - I\beta}{(-\eta_2 + \eta_1)\beta}$$

$$C_2 = \frac{-D_0(-\eta_1 + \lambda - h + \mu)\beta + \theta I\eta_1 + I\beta}{(-\eta_2 + \eta_1)\beta}$$

Therefore; equations (13) & (14) gives the number of diabetics with & without complications at any time t in a population.

Sensitivity Analysis

Consider the following system of O.D.E

$$\frac{dD(t)}{dt} = I(t) - (\lambda - h + \mu)D(t) + \gamma C(t), D(0) = D_0$$

$$\frac{dC(t)}{dt} = \lambda D(t) - (\gamma + \mu + \nu + \delta)C(t), C(0) = C_0 = 0$$

We obtain the critical values as follows;

Assuming a steady state for I(t) (i.e. I(t)=I(independent of time t)), then at critical points the above system reduces to;

$$I - (\lambda - h + \mu)D(t) + \gamma C(t) = 0 \text{ -----(15)}$$

$$\lambda D(t) - (\gamma + \mu + \nu + \delta)C(t) = 0 \text{ -----(16)}$$

Solving for C(t) & D(t) from (15) & (16), we have:

$$C(t) = \frac{\lambda I}{\theta(\lambda - h + \mu) - \gamma\lambda} \quad D(t) = \frac{I\theta}{-\gamma\lambda + \theta(\lambda - h + \mu)}$$

This implies that, the solutions C(t) & D(t) to the O.D.Es will revolve around the critical point values.

LIMITING CASE BEHAVIOUR

Taking the limit of the solutions (13) & (14), i.e.

$$D(t) = C_1 \exp(-\eta_1)t + C_2 \exp(-\eta)t - \frac{\theta I}{\beta}$$

$$C(t) = \frac{1}{\gamma} \left(C_1(-\eta_1 + \lambda - h + \mu)\exp(-\eta_1)t + C_2(-\eta_2 + \lambda - h + \mu)\exp(-\eta_2)t - \frac{(\lambda - h + \mu)}{\beta}(\theta I) - I \right)$$

we have:

$$(i) \quad \lim_{\lambda \rightarrow \infty} D(t) = C_1 \times 0 + C_2 \times 0 - \lim_{\lambda \rightarrow \infty} \frac{((\gamma + \mu + \nu + \delta)I)}{\gamma\lambda - \lambda\theta + h\theta - \mu\theta} = 0$$

$$\lim_{\lambda \rightarrow \infty} C(t) = C_1 \times 0 + C_2 \times 0 - \lim_{\lambda \rightarrow \infty} \left[\frac{(\lambda - h + \mu)(\theta I)}{\beta} + I \right] = \frac{\theta I}{\nu + \mu + \delta}$$

$$(ii) \quad \lim_{\gamma \rightarrow \infty} D(t) = C_1 \times 0 + C_2 \times 0 - \lim_{\gamma \rightarrow \infty} \left(\frac{\theta I}{\beta} \right) = \frac{I}{\mu - h}$$

$$\lim_{\gamma \rightarrow \infty} C(t) = C_1 \times 0 + C_2 \times 0 - \lim_{\gamma \rightarrow \infty} \frac{(\lambda - h + \mu)\theta I}{(\gamma\lambda - \lambda\theta + h\theta - \mu\theta)} - \lim_{\gamma \rightarrow \infty} I = \frac{\lambda I}{\mu - h}$$

$$(iii) \quad \lim_{\delta \rightarrow \infty} D(t) = C_1 \times 0 + C_2 \times 0 - \lim_{\delta \rightarrow \infty} \frac{\theta I}{\beta} = \frac{I}{\lambda - h + \mu}$$

$$\lim_{\delta \rightarrow \infty} C(t) = C_1 \times 0 + C_2 \times 0 - \lim_{\delta \rightarrow \infty} \frac{(\lambda - h + \mu)\theta I}{\gamma\lambda - (\lambda - h + \mu)(\gamma + \mu + \nu + \delta)} - I = 0$$

$$(iv) \quad \lim_{\nu \rightarrow \infty} D(t) = C_1 \times 0 + C_2 \times 0 - \lim_{\nu \rightarrow \infty} \frac{\theta I}{\beta} = \frac{I}{\lambda + \mu - h}$$

$$\begin{aligned} \lim_{\nu \rightarrow \infty} C(t) &= \frac{1}{\gamma} (C_1 \times 0 + C_2 \times 0) - \frac{1}{\gamma} \left(\frac{(\lambda - h + \mu)}{\beta} \theta I - I \right) \\ &= -\frac{1}{\gamma} \left[\frac{(\lambda - h + \mu)I}{-(\lambda - h + \mu)} \right] - \frac{1}{\gamma} I = \frac{I}{\gamma} - \frac{I}{\gamma} = 0 \end{aligned}$$

$$(v) \quad \lim_{\lambda \rightarrow 0} D(t) = C_1 \exp(-\eta_1)t + C_2 \exp(-\eta_2)t - \frac{I}{\mu - h}$$

$$\lim_{\lambda \rightarrow 0} C(t) = \frac{1}{\gamma} (C_1(-\eta_1 - h + \mu) \exp(-\eta_1)t + C_2(-\eta_2 - h + \mu) \exp(-\eta_2)t)$$

where; as $\lambda \rightarrow 0$, then;

$$\theta = \gamma + \mu + \nu + \delta, \quad \sigma = \theta + \mu - h, \quad \beta = (h - \mu)\theta$$

$$\eta_1 = \frac{1}{2}(\theta + \mu - h - \sqrt{(\theta + \mu)^2 - 4\mu\theta}), \quad \eta_2 = \frac{1}{2}(\theta + \mu - h + \sqrt{(\theta + \mu)^2 - 4\mu\theta})$$

$$C_1 = \frac{D_0\beta(-\eta_2 + \mu) - \theta I\eta_2 - I\beta}{(-\eta_2 + \eta_1)\beta}$$

$$C_2 = \frac{-D_0(-\eta_1 + \mu)\beta + \theta I\eta_1 + I\beta}{(-\eta_2 + \eta_1)\beta}$$

$$vi) \quad \lim_{\gamma \rightarrow \infty} \left(\lim_{\lambda \rightarrow 0} D(t) \right) = \lim_{\gamma \rightarrow \infty} \left(C_1 \exp(-\eta_1)t + C_2 \exp(-\eta_2)t + \frac{I}{\mu - h} \right)$$

$$= \frac{I}{\mu - h}$$

$$\lim_{\gamma \rightarrow \infty} \left(\lim_{\lambda \rightarrow 0} C(t) \right) = \lim_{\gamma \rightarrow \infty} \frac{1}{\gamma} [C_1(-\eta_1 + \mu) \exp(-\eta_1)t + C_2(-\eta_2 + \mu) \exp(-\eta_2)t]$$

$$= \lim_{\gamma \rightarrow \infty} \frac{I}{2\gamma\lambda - 2\gamma\lambda - 2\gamma\mu} - 0 = 0$$

$$vii) \quad \lim_{\gamma \rightarrow 0} D(t) = C_1 \exp(-\eta_1)t + C_2 \exp(-\eta_2)t + \frac{I}{\lambda - h + \mu}$$

$$\lim_{\gamma \rightarrow 0} C(t) = \lim_{\gamma \rightarrow 0} \left[\frac{1}{\gamma} (C_1(-\eta_1 + \lambda + \mu) \exp(-\eta_2))t + \lim_{\gamma \rightarrow \infty} \left[\frac{1}{\gamma} C_2(-\eta_2 + \lambda + \mu) \exp(-\eta_2) \right]t + \frac{\theta I}{(\mu + \nu + \delta)} - I \right]$$

$$= \infty$$

where; as $\gamma \rightarrow 0$, then;

$$\theta \rightarrow \mu + \nu + \delta, \quad \sigma \rightarrow 2\mu + \delta + \lambda - h + \nu, \quad \beta \rightarrow -(\lambda - h + \mu)(\mu + \nu + \delta)$$

$$\eta_1 = \frac{1}{2}(\sigma - \sqrt{\sigma^2 + 4\beta}), \quad \eta_2 = \frac{1}{2}(\sigma + \sqrt{\sigma^2 + 4\beta})$$

$$C_1 = \frac{D_0\beta(-\eta_2 + \lambda + \mu) - \theta I\eta_2 - I\beta}{(\sqrt{\sigma^2 + 4\beta})(\mu + \nu + \delta)\lambda}$$

$$C_2 = \frac{-D_0\beta(-\eta_1 + \lambda + \mu) + \theta I\eta_1 + I\beta}{(\sqrt{\sigma^2 + 4\beta})(\mu + \nu + \delta)\lambda}$$

$$viii) \lim_{\delta \rightarrow 0} D(t) = C_1 \exp(-\eta_1)t + C_2 \exp(-\eta_2)t + \frac{(\gamma + \mu + \nu)I}{\gamma\lambda - (\mu + \nu + \lambda)(\lambda - h + \mu)}$$

$$\lim_{\delta \rightarrow 0} C(t) = \frac{1}{\gamma} (C_1(-\eta_1 + \lambda - h + \mu) \exp(-\eta_2)t + C_2(-\eta_2 + \lambda - h + \mu) \exp(-\eta_2)t) - \frac{(\lambda - h + \mu)\theta I}{\beta} - I$$

Where as $\delta \rightarrow 0$;

$$\theta \rightarrow \mu + \nu + \nu, \sigma \rightarrow 2\mu + \nu + \gamma + \lambda - h, \beta \rightarrow \gamma\lambda - (\mu + \nu + \gamma)(\mu + \lambda - h)$$

$$\eta_1 = \frac{1}{2}(\sigma - \sqrt{\sigma^2 + 4\beta}), \eta_2 = \frac{1}{2}(\sigma + \sqrt{\sigma^2 + 4\beta})$$

$$C_1 = \frac{D_0\beta(-\eta_2 + \lambda + \mu) - \theta I\eta_2 - I\beta}{(\eta_1 - \eta_2)\beta}$$

$$C_2 = \frac{-D_0\beta(-\eta_1 + \lambda + \mu) + \theta I\eta_1 + I\beta}{(\eta_1 - \eta_2)\beta}$$

$$ix) \lim_{\gamma \rightarrow \infty} (\lim_{\lambda \rightarrow 0} (\lim_{\delta \rightarrow 0} D(t))) = \lim_{\gamma \rightarrow \infty} (C_1 \exp(-\eta_1)t + C\eta_2 \exp(-\eta_2)t) - \frac{I}{-\mu + h}$$

$$= 0 \times t + 0 \times t - \frac{I}{-\mu + h} = \frac{I}{\mu - h}$$

and $\lim_{\gamma \rightarrow \infty} (\lim_{\lambda \rightarrow 0} (\lim_{\delta \rightarrow 0} C(t)))$

$$= \lim_{\gamma \rightarrow \infty} (\lim_{\lambda \rightarrow 0} (C_1(-\eta_1 + \lambda - h + \mu) \exp(-\eta_1)t + C_2(-\eta_2 + \lambda - h + \mu) \exp(-\eta_2)t) - \frac{(\lambda - h + \mu)\theta I - I\beta}{\beta})$$

$$= \lim_{\gamma \rightarrow \infty} \frac{1}{\gamma} (C_1(-\eta_1 - h + \mu) \exp(-\eta_1)t + C_2(-\eta_2 - h + \mu) \exp(-\eta_2)t - \frac{\mu - h}{\theta(\mu - h)} \theta I - I)$$

$$= 0$$

DISCUSSION ON LIMITING CASE BEHAVIOUR

The following discussion is based on the results of section 2.5

1. From (i) of section 2.5; $\lambda \rightarrow \infty \Rightarrow$ rate of developing complications becomes very high (which may result from lack of optimal glucose control for patients without complications), when this occurs, the number of diabetics without complications $D(t)$ depletes to zero (0) irrespective of the incidence rate of diabetes. On the other hand, $C(t)$ approaches $\frac{\theta I}{\nu + \mu + \delta}$, which depends only on $I, \gamma, \mu, \delta, \nu, \& \theta = \gamma + \mu + \nu + \delta$. This implies that; with very high (uncontrollable) rate of developing complications, the number of diabetics without complications, $D(t)$, drops to zero(0), while the number of diabetics with complications $C(t)$, stabilizes at $\frac{\theta I}{\mu + \delta + \nu}$, this translate to the need to reduce I , since reducing $\frac{\theta I}{\mu + \delta + \nu}$ will not have practical benefit.

2. From (ii) of section 2.5; $\gamma \rightarrow \infty \Rightarrow$ recovery from complications becomes very high (which may result from intensive recovery programme for patients with complications), when this occurs, the number of diabetics without complications, $D(t)$, approaches $\frac{I}{\mu - h}$, which depends only on $I, \mu \& h$. On the other hand $C(t)$ vanishes to zero,

irrespective of the incidences I . This implies that; with high rate of recovery from complications, γ , the number of diabetics with complications $C(t)$ drops to zero, while the number of diabetics without complications $D(t)$ stabilizes at $\frac{I}{\mu - h}$, this translate to the need to regulate I and h to bring down $D(t)$ and $C(t)$ respectively.

3. From (iii) of section 2.5; $\delta \rightarrow \infty \Rightarrow$ Mortality rate due to complications becomes very high (*which may result from lack of adequate control for complications*), when this occurs, $C(t)$ drops to zero, irrespective of the incidence, I , while $D(t)$ stabilizes at $\frac{I}{\lambda - h + \mu}$, which depends only on I, λ, h & μ . This implies that; with very high mortality rate due to complications, $C(t)$ reduces to zero (0), while $D(t)$ stabilizes at $\frac{I}{\lambda - h + \mu}$, this translate to the need to regulate I and h to bring down $D(t)$ and $C(t)$ respectively.

4. From (iv) of section 2.5; $\nu \rightarrow \infty \Rightarrow$ Rate of developing disability becomes very high (*which may result from deterioration of complications*), when this occurs, $C(t)$ drops to zero, while $D(t)$ stabilizes at $\frac{I}{\lambda - h + \mu}$, which depends on I, λ, h & μ . This implies that; with very high rate of disability, $C(t)$ drops to zero, while $D(t)$ stabilizes at $\frac{I}{\lambda - h + \mu}$, this translates to the need to regulate I and h to bring down $D(t)$ and $C(t)$ respectively.

5. From (v) of section 2.5; $\lambda \rightarrow 0 \Rightarrow$ Rate of developing complications approaches zero, when this occurs, $D(t)$ stabilizes at; $C_1 \exp(-\eta_1)t + C_2 \exp(-\eta_2)t - \frac{I}{\mu - h}$

while $C(t)$ stabilizes at; $C_1(-\eta_1 - h + \mu)\exp(-\eta_1)t + C_2(-\eta_2 - h + \mu)\exp(-\eta_2)t$. This implies that; as the rate of developing complications approaches zero, $D(t)$ depends on I , and regulated by μ, γ, δ, h & ν , while $C(t)$ depends only on μ, γ, δ, h & ν . In either case, this translates to the need to regulate I and h to bring down $D(t)$.

6. From (vi) of section 2.5; $\gamma \rightarrow \infty$ & $\lambda \rightarrow 0 \Rightarrow$ very high rate of recovery from complications and vanishing rate of complications, when this occurs, $D(t)$ stabilizes at $\frac{I}{\mu - h}$, while $C(t)$ approaches zero. This implies that, with aggressive and sustained recovery programme for patients with complications, and vanishing rate of developing complications, $C(t)$ drops to zero, while $D(t)$ stabilizes at $\frac{I}{\mu - h}$, which depends on I, h & μ . This translates to the need for regulating I and h to bring down $D(t)$ and $C(t)$ respectively.

7. From (vii) of section 2.5; $\gamma \rightarrow 0 \Rightarrow$ Rate of recovery from complications approaches zero(0), when this occurs, $C(t)$ approaches ∞ , while $D(t)$ approaches $C_1 \exp(-\eta_1)t + C_2 \exp(-\eta_2)t + \frac{I}{\lambda - h + \mu}$. This implies that, with vanishing rate of recovery (γ) from complications, $C(t)$ becomes too large (∞), this is because of injection by λ . On the other hand, $D(t)$ stabilizes at $C_1 \exp(-\eta_1)t + C_2 \exp(-\eta_2)t + \frac{I}{\lambda - h + \mu}$, which depends on $I, \mu, \lambda, \nu, \delta$ & h .

This translates to the need for regulating I and h to bring down $D(t)$ and $C(t)$ respectively.

8) From (viii) of section 2.5; $\delta \rightarrow 0 \Rightarrow$ Rate of mortality due to complications vanishes, when this occurs, the number diabetics without complications D(t) and the number of diabetics with complications C(t) approaches:

$$C_1 \exp(-\eta_1)t + C_2 \exp(-\eta_2)t + \frac{(\gamma + \mu + \nu)I}{\gamma\lambda - (\mu + \nu + \lambda)(\lambda - h + \mu)}$$

and

$$\frac{1}{\gamma}(C_1(-\eta_1 + \lambda - h + \mu)\exp(-\eta_2)t + C_2(-\eta_2 + \lambda - h + \mu)\exp(-\eta_2)t) - \frac{(\lambda - h + \mu)\theta I}{\beta} - I$$

respectively. This implies that, as the rate of mortality due to complications approaches zero, C(t) & D(t) reduces to the definite values shown above,

which are both functions of $I, \mu, \lambda, \gamma, h$ & ν . This translates to the need to

regulate I, h to bring down D(t) and C(t) respectively.

9) From (ix) of section 2.5; $\gamma \rightarrow \infty, \lambda \rightarrow 0$ & $\delta \rightarrow 0 \Rightarrow$ Very high rate of recovery from complications, decreasing rate of developing complications & mortality due to complications. When this occurs, the number of diabetics without complications D(t) approaches $\frac{I}{\mu - h}$, while the number of diabetics with complications drops to zero.

This implies that, with very high recovery rate (*which can be as a result of rigorous recovery programme for patients with complications*), decreasing rate of developing complications and decreasing mortality rate due to complications,

C(t) drops to zero, while D(t) stabilizes at $\frac{I}{\mu - h}$. This translates to the need for regulating I and h to bring down D(t) and

C(t) respectively.

From the above discussion, the results suggest that; to Control diabetes, we need to reduce the incidence of diabetes I and improve the rate of retardation of transition to diabetes with complication. This will, respectively reduce cases of diabetes incidence and manage sufferers to extinction.

CONCLUSION

From the above discussion, we conclude as follows;

The system of equations describing the dynamics of diabetes in the susceptible sub-population suggest that; we need to control the incidence I and improve the rate of inhibition, h for transition from diabetes without complication to diabetes with complication.

This entails going further in research to;

1. Look into the dynamics of the genetics of transmission of the diabetic gene, to investigate how to reduce the spread (and hence the incidence I) of diabetes
2. Look into the effect of physical exercise and/or dieting on the dynamics of glucose metabolism, this will give an insight on how to manage diabetic patients.

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