Mathematical Model For Diabetic To Be On Dialysis

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Abstract: Diabetes is the disease in which sugar level fluctuates. The clinical purification of the blood is the only possible through dialysis in the advance stage of type 2 diabetes. In this paper, a mathematical model for diabetic and to choose dialysis as comfortable treatment has been formulated as a system of non-linear ordinary differential equation. The model comprises of susceptible (\(S\)), diabetic (\(D\)), dialysis (\(D_t\)) and temporary recovery (\(ID\)) subgroups. The threshold for the opting dialysis by diabetic individuals is computed. The stability of the equilibrium points are discussed. The proposed model is visualized through simulation.

Index Terms: Diabetic, Dialysis, System of non-linear ordinary differential equation, Threshold, Stability.

1 INTRODUCTION
Disease is an abnormal condition when sugar level of individual fluctuates. Diseases can be distributed as communicable and non-communicable (https://en.wikipedia.org/wiki/Disease). The World Health Organization (WHO) has recognized mainly four types of non-communicable disease: cancer, cardiovascular disease (e.g. heart attack), chronic respiratory disease (e.g. asthma) and diabetes mellitus (http://www.who.int/mediacentre/factsheets/fs355/en/). In this proposed paper, we will focus on diabetes. It can be either genetic or caused due to the insufficient production of insulin by the pancreas or it may occur if the cells of the body are not responding to the insulin produced. Symptoms of diabetes include increase in thirst, urination and hunger. It was estimated that more than 382 million individuals throughout the world were the victim of diabetes in 2013 (https://www.diabetes.co.uk/). Diabetes is classified into type 1, type 2 and gestational diabetes. Type 1 diabetes occurs while immune system destroys cells in pancreas called beta cells and they make insulin. Genes and environmental factors are the causes of type 1 diabetes. Genes and life-style are responsible for causing type 2 diabetes as well as gestational diabetes which develops during pregnancy. Diabetes often causes complication in kidneys. If the kidney does not work properly, the only treatment option available for the purification of blood is dialysis. Dialysis changes the normal blood-filtering of the kidney, so it is also known as Renal Replacement Therapy (RRT) (https://www.medicalnewstoday.com/articles/152902.php). This treatment last from 2.5 to 4.5 hours (https://www.medicinenet.com/dialysis/article.htm). The United States renal data system (USRDS) reported that a patient of dialysis of the age 40-44 years can receive dialysis approximately for 8 years whereas the age of 60-64 years individuals can receive approximately for 4.5 years in the expected life span (https://www.medicinenet.com/dialysis/article.htm).


### Table 1: Notation and its parametric values

<table>
<thead>
<tr>
<th>Notation</th>
<th>Parametric Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>(S(t))</td>
<td>The susceptible class comprising of individuals who have normal</td>
</tr>
<tr>
<td>(D_s(t))</td>
<td>The diabetes class i.e., who have diabetes</td>
</tr>
<tr>
<td>(D_t(t))</td>
<td>The dialysis class i.e., who need to dialysis</td>
</tr>
<tr>
<td>(R(t))</td>
<td>The recover class i.e., who recover from diabetes and dialysis</td>
</tr>
<tr>
<td>(N(t))</td>
<td>Total population at any time t</td>
</tr>
<tr>
<td>(B)</td>
<td>The recruitment number (Birth rate)</td>
</tr>
<tr>
<td>(\mu)</td>
<td>The death rate</td>
</tr>
<tr>
<td>(\alpha)</td>
<td>Diseases induced death rate</td>
</tr>
<tr>
<td>(\beta)</td>
<td>The rate of individuals who have diabetes</td>
</tr>
<tr>
<td>(\gamma_1)</td>
<td>The rate of individuals who need to be on dialysis</td>
</tr>
<tr>
<td>(\gamma_2)</td>
<td>The rate of individuals who recovered from diabetes</td>
</tr>
<tr>
<td>(\eta)</td>
<td>The rate of individuals moving to temporary recovery class due to dialysis</td>
</tr>
<tr>
<td>(\delta)</td>
<td>The rate of individuals who have need to be on dialysis</td>
</tr>
</tbody>
</table>

2 MATHEMATICAL MODEL
Here, we formulate a mathematical model for diabetic to be on dialysis. The notations along with its parametric values are shown in table 1. The transmission diagram of diabetic to be on dialysis is shows in figure 1. In figure 1 \(S(t)\) denotes the number of susceptible individuals. Out of this, some individuals who have diabetes \(D_s(t)\) with the rate \(\beta\) and
some individuals who need to be on dialysis \((D_t(t))\) with the rate \(\delta\). The number of diabetic individuals opting for dialysis with the rate \(\gamma_1\) \((R(t))\) denotes the number of individuals moving to temporary recovery class due to dialysis with the rate \(\eta\) and from diabetic with the rate \(\gamma_2\). \(\mu\) denotes the death rate means individuals who do not have diabetes or sugar problem or who do not opt for dialysis or death and \(\alpha\) denote the diseases induced death rate.

![Diagram](image)

Fig. 1. Transmission of diabetic to be on dialysis

The model can be described by the nonlinear system of differential equation as

\[
\begin{align*}
\frac{dS}{dt} &= B - \beta SD - \delta SD - \mu S \\
\frac{dD_2}{dt} &= \beta SD - (\mu + \alpha)D_2 - \gamma_1 D_2 - \gamma_2 D_2 \\
\frac{dD_1}{dt} &= \gamma_1 D_2 + \delta SD - \eta D_1 - (\mu + \alpha)D_1 \\
\frac{dR}{dt} &= \gamma_2 D_2 + \eta D_1 - \mu R
\end{align*}
\]

(1)

where \(S + D_2 + D_1 + R = N\)

Adding all the equations in (1), we get

\[
\frac{dN}{dt} = B - \beta SD - \delta SD - \mu S + \beta SD - (\mu + \alpha)D_2 - \gamma_1 D_2 - \gamma_2 D_2 - \eta D_1 - (\mu + \alpha)D_1 - \mu R
\]

This gives \(\limsup_{t \to \infty}(S + D_2 + D_1 + R) \leq \frac{B}{\mu}\)

Therefore, the feasible region for the solution of (1) is

\[
A = \left\{ (S + D_2 + D_1 + R) \mid (S + D_2 + D_1 + R) \leq \frac{B}{\mu}, S > 0, D_2 > 0, D_1 \geq 0, R > 0 \right\}
\]

The set  \(A\) is positive invariant for any time \(t > 0\).

To obtain equilibrium point for \(E_0\) for transmission of disease in different compartment, we have

\[
\begin{align*}
\frac{dS}{dt} &= \beta SD - \mu S = 0 \\
\frac{dD_2}{dt} &= \beta SD - (\mu + \alpha)D_2 - \gamma_1 D_2 - \gamma_2 D_2 = 0 \\
\frac{dD_1}{dt} &= \gamma_1 D_2 + \delta SD - \eta D_1 - (\mu + \alpha)D_1 = 0 \\
\frac{dR}{dt} &= \gamma_2 D_2 + \eta D_1 - \mu R = 0
\end{align*}
\]

(2)

For \(D_2 = D_1 = R = 0\), the dialysis free equilibrium is \(E_0 = (B, 0, 0, 0)\). Now, let \(\dot{X} = (R_1, D_1, D_2, S)\), where dash denotes derivative with respect to time. Then, the system (1) can be written as

\[
X' = \frac{dX}{dt} = F(X) - V(X), \text{ where}
\]

\[
F(X) = \begin{bmatrix}
\beta SD \\
\delta SD \\
0 \\
0
\end{bmatrix},
V(X) = \begin{bmatrix}
\gamma_2 D_2 + (\mu + \alpha)D_2 \\
-\gamma_1 D_2 + \eta D_1 + (\mu + \alpha)D_1 \\
-\gamma_2 D_2 + \eta D_1 + \mu R \\
\beta SD + \delta SD + \mu S
\end{bmatrix}
\]

Now, we find \(f\) and \(v\) by the derivative of \(F\) and \(V\) at equilibrium point \(E_0\).

Here, \(f\) and \(v\) are 4\times4 matrix define as

\[
f = \left[\frac{\partial F(X_0)}{\partial X}ight], \quad v = \left[\frac{\partial V(X_0)}{\partial X}\right]
\]

where \(i, j = D_2, D_1, R, S\)

\[
\begin{bmatrix}
\beta \mu & 0 & 0 & \beta D_2 \\
0 & \beta \mu & 0 & D_1 \\
0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0
\end{bmatrix},
\begin{bmatrix}
\gamma_1 + \gamma_2 + \mu + \alpha & 0 & 0 & 0 \\
0 & \gamma_1 & 0 & 0 \\
\gamma_2 + \mu + \alpha & 0 & 0 & 0 \\
\gamma_2 + \mu + \alpha & 0 & 0 & 0
\end{bmatrix}
\]

Now, we find \(v^{-1}\) and \(f \cdot v^{-1}\) at an equilibrium point \(E_0\).

\[
v^{-1} = \begin{bmatrix}
1 \\
\gamma_1 \\
(\gamma_1 + \gamma_2 + \mu + \alpha)(\mu + \alpha) & 1 \\
\gamma_2 + \mu + \alpha & 0 & 0 & 0 \\
B(\beta + \beta + \delta Y_1) & \delta B Y_1 & \delta B & 0 & 0 \\
\mu + \alpha & \mu + \alpha & \mu + \alpha & \mu + \alpha & \mu + \alpha
\end{bmatrix}
\]

\[
f \cdot v^{-1} = \begin{bmatrix}
\frac{\beta B}{\mu} & 0 & 0 & 0 \\
\delta B Y_1 & 0 & 0 & 0 & 0
\end{bmatrix}
\]

The basic reproduction number \(R_0\) is the spectral radius of matrix \(f \cdot v^{-1}\) and is given by

\[
R_0 = \frac{B(\beta + \beta + \delta Y_1 + \delta Y_2 + \delta \mu + \delta \alpha)}{\mu + \alpha}
\]

On solving, the set of equation (1), we get two more equilibrium points

- \(E_1 = (S, 0, D_1, R)\) when individual does not have diabetes, where,

\[
S = \frac{\eta + \mu + \alpha}{\delta}, \quad D_1 = 0, \quad D_2 = \frac{\delta B - \mu(\mu + \alpha)}{\delta (\mu + \alpha)}, \quad R = \frac{\eta (\delta B - \mu (\mu + \alpha))}{\delta (\mu + \alpha)}
\]

- \(E^* = (S', D_2', D_1', R')\) when all exists, where,
\[ S^* = \gamma_1 + \gamma_2 + \mu + \alpha \]
\[ D^*_a = \beta(\mu + \eta + \alpha) \]
\[ D^*_b = \beta(\mu + 2\alpha + \gamma_1 + \gamma_2 + \mu + \alpha(\gamma_1 + \gamma_2 + \eta + \alpha)) \]
\[ D^*_c = \beta(\mu + 2\alpha + \gamma_1 + \gamma_2 + \mu) + \alpha(\gamma_1 + \gamma_2 + \eta + \alpha) \]
\[ D^*_d = \beta(\mu + 2\alpha + \gamma_1 + \gamma_2 + \mu) + \alpha(\gamma_1 + \gamma_2 + \eta + \alpha) \]
\[ R^* = \beta(\mu + 2\alpha + \gamma_1 + \gamma_2 + \mu) + \alpha(\gamma_1 + \gamma_2 + \eta + \alpha) \]

3 STABILITY ANALYSIS
Here, we discuss the local and global stability of the proposed model.

3.1 Local Stability
If all the eigenvalues of the Jacobin matrix of the system (1) have negative real part then equilibrium point is locally stable.

Theorem 1. The unique equilibrium points \( E_0 = (S,0,0,0) \) and \( E_1 = (S,0,D_T,R) \) of the transmission of diabetic to be on dialysis model is locally asymptotically stable.

Proof. At point \( E_0 \), the Jacobean matrix takes the form

\[ J_0 = \begin{bmatrix} -\mu & -\beta B & -\delta B & 0 \\ 0 & \beta B & \gamma_1 - \gamma_2 - \mu - \alpha & 0 \\ 0 & \gamma_1 & \delta B & -\eta - \mu - \alpha \\ 0 & 0 & \eta & -\mu \end{bmatrix} \]

\[ \text{trace}(J) = -\mu + \beta B + \delta B \gamma_1 - \gamma_2 - 2\alpha - 4\mu < 0 \]
Therefore, \( E_0 \) is locally stable.

At point \( E_1 = (S,0,D_T,R) \), the Jacobean matrix takes the form,

\[ J_1 = \begin{bmatrix} -\mu - (\eta + \alpha) & -\beta (\eta + \alpha) & \delta (\eta + \alpha) & 0 \\ 0 & \beta (\eta + \alpha) & \gamma_1 - \gamma_2 - \mu - \alpha & 0 \\ 0 & \delta (\eta + \alpha) & \gamma_1 & \eta - \mu \\ 0 & 0 & \eta & -\mu \end{bmatrix} \]

\[ \text{trace}(J) = -\mu - (\eta + \alpha) + \beta (\eta + \alpha) + \delta (\eta + \alpha) - \gamma_1 - \gamma_2 - 3\alpha - 3\mu < 0 \]
Therefore, \( E_1 \) is locally stable.

Theorem 2. The unique positive equilibrium point \( E^* \) is locally asymptotically stable with the condition that \( X_1 > 0 \) if and only if \( \beta(\eta + \alpha) > \delta(\gamma_1 + \gamma_2 + \mu + \alpha) \).

Proof. The Jacobean matrix of system (1) at endemic point \( E^* \) is as follows:

\[ J^* = \begin{bmatrix} -x_1 & -\beta S^* & -\delta S^* & 0 \\ \beta D^*_a & -x_2 & 0 & 0 \\ -x_3 & 0 & 0 & 0 \\ 0 & x_2 & x_1 & -\mu \end{bmatrix} \]

where

\[ x_1 = \beta D^*_a + \delta D^*_b + \mu, x_2 = \gamma_1 + \gamma_2 + \mu + \alpha - \beta S^*, x_3 = \eta + \mu + \alpha - \delta S^* \]

The characteristic polynomial of the above Jacobean matrix is

\[ \lambda^3 + X_1^2 + X_2 + \mu(\gamma_1 + \gamma_2 + \alpha + \beta S^*) + \delta D^*_b S^* + x_1 \beta D^*_a S^* + x_1 x_3 \]

Where

\[ X_1 = \mu + x_1 + x_2 + x_3 \]
\[ X_2 = \mu(x_1 + x_2 + x_3) + \delta D^*_b S^* + x_1 x_3 + x_2 x_3 + \beta^2 D^*_b S^* + x_1 x_2 \]
\[ X_3 = \mu(\delta^2 D^*_b S^* + \beta^2 D^*_b S^*) + x_1 x_3 + x_2 x_3 + \gamma_1(\delta + \beta) + \beta D^*_a S^* + \delta^2 D^*_b S^* + x_1 x_3 \]

Here, \( X_1 > 0, X_2 > 0, X_3 > 0 \) and satisfy the condition of Routh-Hurwitz criterion (Routh E.J. 1877) provided \( X_2 > 0 \).

Therefore, \( E^* \) is locally stable.

3.2 Global Stability

Theorem 3. If \( \det(I - f \cdot v^{-1}) > 0 \) then equilibrium point \( E_0 \) is globally stable.

Proof.

\[ \det(I - f \cdot v^{-1}) = \begin{vmatrix} 1 - \frac{\beta B}{\mu(\gamma_1 + \gamma_2 + \mu + \alpha)} & 0 & 0 \\ -\frac{\delta B}{\mu(\gamma_1 + \gamma_2 + \mu + \alpha)} & 1 - \frac{\delta B}{\mu(\mu + \alpha)} & 0 \\ 0 & 0 & 0 \end{vmatrix} \]

\[ = 1 - R_0 \]
\[ = 1 - 0.4660 \]
\[ = 0.534 > 0 \]
Thus, \( E_0 \) is globally stable.

Theorem 4: If first order derivative of Lyapunov function is less than or equal to zero then endemic point \( E_1 \) and \( E^* \) are globally asymptotically stable.

Proof: Consider, the Lyapunov function for \( E_1 = (S,0,D_T,R) \)

\[ L(t) = S(t) + D^*_a(t) + D^*_b(t) \]
\[ L'(t) = S'(t) + D^*_a'(t) + D^*_b'(t) \]
\[ = B - \mu S - \gamma_2 D^*_b - (\mu + \alpha) D^*_b - \eta D^*_b - (\mu + \alpha) D^*_b \]
\[ \leq B - \mu S - \gamma_2 D^*_b - (\mu + \alpha) D^*_b - \eta D^*_b - (\mu + \alpha) D^*_b \]
\[ = -\gamma_2 D^*_b - \eta D^*_b - (\mu + \alpha) D^*_b - (\mu + \alpha) D^*_b \]
\[ \leq 0 \]
Hence, $E_i$ is globally stable.

Consider, the Lyapunov function for $E^* = (S^*, D^*_B, D^*_I, R^*)$

$$L(t) = \frac{1}{2} \left[ (S - S^*)^2 + (D_B - D^*_B)^2 + (D_I - D^*_I)^2 + (R - R^*)^2 \right]$$

$$L'(t) = [S - S^* + D_B - D^*_B + D_I - D^*_I + (R - R^*)] [S^* + D^*_B + D^*_I + R^*]$$

$$= \left[ (S - S^*) + (D_B - D^*_B) + (D_I - D^*_I) + (R - R^*) \right] B - \mu S - (\mu + \alpha) D_B - (\mu + \alpha) D_I - \mu R$$

$$= -\mu \left[ (S - S^*) + (D_B - D^*_B) + (D_I - D^*_I) + (R - R^*) \right] B + S^* + D^*_B + D^*_I + R^*$$

$$\leq 0$$

Here, we write, $B = \mu S^* + (\mu + \alpha) D^*_B + (\mu + \alpha) D^*_I + \mu R^*$

Hence, $E^*$ is globally stable.

### 4 SENSITIVITY ANALYSIS

The sensitivity analysis for all model parameters is discussed in this section. The normalized sensitivity index of the parameters is computed by using formula (Shah et al. 2017)

$$V_{\theta}^{R_i} = \frac{\partial R_i}{\partial \theta} \cdot \frac{\partial \theta}{\partial R_i}$$

**TABLE 2 SENSITIVITY ANALYSIS**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Sign</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>$B$</td>
<td>+</td>
<td>Prone to be diabetic if maternal history speaks of diabetes.</td>
</tr>
<tr>
<td>$\beta$</td>
<td>+</td>
<td>High level of glucose and insufficient production of insulin results diabetes.</td>
</tr>
<tr>
<td>$\gamma_1 / \gamma_2$</td>
<td>-</td>
<td>More diabetic individuals need to opt for dialysis at same time.</td>
</tr>
<tr>
<td>$\eta$</td>
<td>0</td>
<td>No effect</td>
</tr>
<tr>
<td>$\delta$</td>
<td>+</td>
<td>For severe diabetic individual only alternative is dialysis</td>
</tr>
<tr>
<td>$\mu$</td>
<td>-</td>
<td>More individuals take prevention</td>
</tr>
<tr>
<td>$\alpha$</td>
<td>-</td>
<td>Death is not related to diabetes or dialysis</td>
</tr>
</tbody>
</table>

, where $\theta$ denotes model parameters.

### 5 NUMERICAL SIMULATION

In this section, we will study the numerical results of all compartments.

Figure 2 shows that the number of susceptible individuals decreases with the time as individuals suffer from diabetes or they need to go for dialysis. Almost 47 diabetic patients go for dialysis approximately in a year. On the other hand, 24 individuals recover temporarily in 1.6 years.

Figure 3 on directed graph, suggests that the diabetic individuals opts for dialysis after 5-years.

Figure 4 shows the effect of the rate of individuals moving to temporary recovery class due to dialysis ($\eta$). When $\eta$ increases from 0.3% to 30% then the rate of temporary recovered individuals is increased to 33.83% and then they decrease after almost 1.8 years.

Figure 5 shows that if the rate of individuals from diabetes to dialysis ($\gamma_1$) is increased from 20% to 40% then the number of individuals opting for dialysis will increase from 47 to 55. After 10 years, the numbers of individuals get stable.
Figure 6 shows that if the rate of individuals from diabetes to temporary recover $\gamma_1$ is increased from 12% to 32% then the number of temporary recovered individuals will increase from 19 to 30. After 10 years, the number of individuals gets stable.

6 CONCLUSION
Here, a non-linear mathematical model for diabetic to be on dialysis is formulated. The system is locally and globally asymptotically stable at equilibrium point $E_0$. Making few lifestyle changes can lower the risk of sugar problem. To prevent diabetes, manage your weight, exercise regularly, eat a balanced healthy diet, reduce intake of processed foods, limit your alcohol intake, quit smoking, control your blood pressure etc. If you have diabetes and kidneys ease, it is important to maintain blood sugar level. Using the numerical values given in the table (1), we computed that 46.6% diabetic individuals have to opt for dialysis.

7 ACKNOWLEDGMENT
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