Mathematical Model For Diabetic To Be On Dialysis

Nita H. Shah, Foram M. Suthar, Moksha H. Satia , Foram A. Thakkar

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 ( ), diabetic ( ), dialysis ( ) and temporary recovery ( ) 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).

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This treatment results into different side effects like low blood pressure, nausea and vomiting, dry or itchy skin, restless leg syndrome, muscle cramping and many more (https://www.medicinenet.com/dialysis/article.htm). Boutayab et al. (2004) has carried out research entitled “A mathematical model for the burden of diabetes and its complications”. Cobelli et al. (2002) has carried out research entitled “An integrated mathematical model of the dynamics of blood glucose and its hormonal control.” Waniewski et al. (1991) has studied “A comparative analysis of mass transport models in peritoneal dialysis.” Pier Giorgio Fabietti et al (2006) has done research entitled “Control oriented model of insulin and glucose dynamics in type 1 diabetics”.

TABLE 1
NOTATION AND ITS PARAMETRIC VALUES

Notation		Parametric Values
$S(t)$	The susceptible class comprising of individuals who have normal	100
$D_B(t)$	The diabetes class i.e., who have diabetes	35
$D_I(t)$	The dialysis class i.e., who need to dialysis	25
$R(t)$	The recover class i.e., who recover from diabetes and dialysis	18
$N(t)$	Total population at any time t	200
B	The recruitment number (Birth rate)	0.40
μ	The death rate	0.35
α	Diseases induced death rate	0.10
β	The rate of individuals who have diabetes	0.18
γ_1	The rate of individuals who need to be on dialysis	0.30
γ_2	The rate of individuals who recovered from diabetes	0.22
η	The rate of individuals moving to temporary recovery class due to dialysis	0.003
δ	The rate of individuals who have need to be on dialysis	0.1

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 $(D_B(t))$ with the rate β and some individuals who need to be on dialysis $\left(D_I(t)\right)$ with the rate δ. The number of diabetic individuals opting for dialysis with the rate γ_1. $\left(R(t)\right)$ denotes the number of individuals moving to temporary recovery class due to dialysis with the rate η and from diabetic with the rate γ_2. μ denotes the death rate means individuals who do not have diabetes or sugar problem or who do not opt for dialysis or death and α denote the diseases induced death rate.

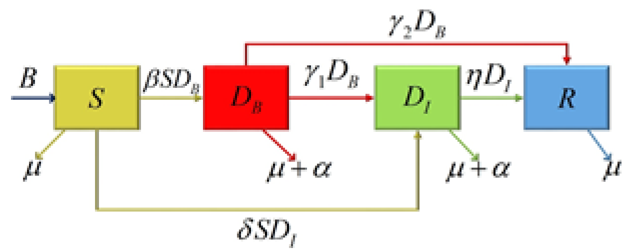

Fig. 1. Transmission of diabetic to be on dialysis

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

$$\begin{aligned}
\frac{dS}{dt} &= B-\beta SD_B-\delta SD_I-\mu S\\
\frac{dD_B}{dt} &= \beta SD_B-(\mu+\alpha)D_B-\gamma_1 D_B-\gamma_2 D_B\\
\frac{dD_I}{dt} &= \gamma_1 D_B+\delta SD_I-\eta D_I-(\mu+\alpha)D_I\\
\frac{dR}{dt} &= \gamma_2 D_B+\eta D_I-\mu R
\end{aligned} \tag{1}$$

where $S+D_B+D_I+R=N$

Adding all the equations in (1), we get

$$\begin{aligned}
\frac{dN}{dt} &= B-\beta SD_B-\delta SD_I-\mu S+\beta SD_B-(\mu+\alpha)D_B-\gamma_1 D_B-\gamma_2 D_B+\gamma_1 D_B+\delta SD_I\\
&\quad -\eta D_I-(\mu+\alpha)D_I+\gamma_2 D_B+\eta D_I-\mu R\\
&= B-\mu(S+D_B+D_I+R)-\alpha(D_B+D_I)
\end{aligned}$$

This gives $\limsup\limits_{t\to\infty}(S+D_B+D_I+R)\le\dfrac{B}{\mu}$.

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

$$A=\left\{\begin{matrix}(S+D_B+D_I+R):(S+D_B+D_I+R)\le\dfrac{B}{\mu};\\ S>0, D_B\ge 0, D_I\ge 0, R>0\end{matrix}\right\}.$$

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

$$\begin{aligned}
&B-\beta SD_B-\delta SD_I-\mu S=0\\
&\beta SD_B-(\mu+\alpha)D_B-\gamma_1 D_B-\gamma_2 D_B=0\\
&\gamma_1 D_B+\delta SD_I-\eta D_I-(\mu+\alpha)D_I=0\\
&\gamma_2 D_B+\eta D_I-\mu R=0
\end{aligned} \tag{2}$$

For $D_B=D_I=R=0$, the dialysis free equilibrium is $E_0=\left(\dfrac{B}{\mu},0,0,0\right)$.

Now, let $X'=(R,D_I,D_B,S)'$, where dash denotes derivative with respect to time. Then, the system (1) can be written as

$X'=\dfrac{dX}{dt}=F(X)-V(X)$, where

$$F(X)=\begin{bmatrix}\beta SD_B\\ \delta SD_I\\ 0\\ 0\end{bmatrix},\ V(X)=\begin{bmatrix}\gamma_2 D_B+\gamma_1 D_B+(\mu+\alpha)D_B\\ -\gamma_1 D_B+\eta D_I+(\mu+\alpha)D_I\\ -\gamma_2 D_B+\eta D_I+\mu R\\ \beta SD_B+\delta SD_I+\mu S\end{bmatrix}$$

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

Here, f and v are 4×4 matrix define as

$f=\left[\dfrac{\partial F_i(X_0)}{\partial X_j}\right]$, $v=\left[\dfrac{\partial V_i(X_0)}{\partial X_j}\right]$ where $i,j=D_B,D_I,R,S$

$$f=\begin{bmatrix}\beta\frac{B}{\mu} & 0 & 0 & \beta D_B\\ 0 & \delta\frac{B}{\mu} & 0 & \frac{B}{\mu}D_I\\ 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0\end{bmatrix},V=\begin{bmatrix}\gamma_1+\gamma_2+\mu+\alpha & 0 & 0 & 0\\ -\gamma_1 & \mu+\alpha & 0 & 0\\ -\gamma_2 & -\eta & \mu & 0\\ \beta\frac{B}{\mu} & \delta\frac{B}{\mu} & 0 & \beta D_B+\delta D_I+\mu\end{bmatrix}$$

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

$$v^{-1}=\begin{bmatrix}\dfrac{1}{\gamma_1+\gamma_2+\mu+\alpha} & 0 & 0 & 0\\ \dfrac{\gamma_1}{(\gamma_1+\gamma_2+\mu+\alpha)(\mu+\alpha)} & \dfrac{1}{\mu+\alpha} & 0 & 0\\ \dfrac{\gamma_2\mu+\gamma_2\alpha+\eta\gamma_1}{(\mu+\alpha)(\gamma_1+\gamma_2+\mu+\alpha)\mu} & \dfrac{\eta}{(\mu+\alpha)\mu} & \dfrac{1}{\mu} & 0\\ -\dfrac{B(\beta\mu+\beta\alpha+\delta\gamma_1)}{\mu^2(\mu+\alpha)(\gamma_1+\gamma_2+\mu+\alpha)} & -\dfrac{\delta B}{\mu^2(\mu+\alpha)} & 0 & \dfrac{1}{\mu}\end{bmatrix}$$

$$f\cdot v^{-1}=\begin{bmatrix}\dfrac{\beta B}{\mu(\gamma_1+\gamma_2+\mu+\alpha)} & 0 & 0 & 0\\ \dfrac{\delta B\gamma_1}{\mu(\mu+\alpha)(\gamma_1+\gamma_2+\mu+\alpha)} & \dfrac{\delta B}{\mu(\mu+\alpha)} & 0 & 0\\ 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0\end{bmatrix}$$

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

$$R_0=\frac{B(\beta\mu+\beta\alpha+\delta\gamma_1+\delta\gamma_2+\delta\mu+\delta\alpha)}{\mu(\mu+\alpha)(\gamma_1+\gamma_2+\mu+\alpha)}$$

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

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

$$S=\frac{\eta+\mu+\alpha}{\delta},\ D_B=0,\ D_I=\frac{\delta B-\mu(\eta+\mu+\alpha)}{\delta(\eta+\mu+\alpha)},\ R=\frac{\eta(\delta B-\mu(\eta+\mu+\alpha))}{\delta\mu(\eta+\mu+\alpha)}$$

- $E^*=(S^*,D_B^*,D_I^*,R^*)$ when all exists, where,

$$S^* = \frac{\gamma_1+\gamma_2+\mu+\alpha}{}$$

$$D_B^* = \frac{(\beta B-\mu(\gamma_1+\gamma_2+\mu+\alpha))\cdot(\beta(\mu+\eta+\alpha) -\delta(\gamma_1+\gamma_2+\mu+\alpha))}{\beta\left\{\begin{array}{l}\beta(\mu(\eta+2\alpha+\gamma_1+\gamma_2+\mu)+\alpha(\gamma_1+\gamma_2+\eta+\alpha)\\ +\eta(\gamma_1+\gamma_2))-\delta(\mu(\gamma_1+2\gamma_2+2\alpha+\mu)\\ +\alpha(\gamma_1+2\gamma_2+\alpha)+\gamma_2(\gamma_1+\gamma_2))\end{array}\right\}}$$

$$D_I^* = \frac{\gamma_1(\beta B-\mu(\gamma_1+\gamma_2+\mu+\alpha))}{\left\{\begin{array}{l}\beta(\mu(\gamma_1+\gamma_2+\mu+2\alpha+\eta)+\alpha(\gamma_1+\gamma_2+\eta+\alpha)+\eta\gamma_2)\\ -\delta(\mu(\gamma_1+2\gamma_2+\mu+\alpha)+\alpha(\gamma_1+\gamma_2+\alpha)+\gamma_2(\gamma_1+\gamma_2))\end{array}\right\}}$$

$$R^* = \frac{(\beta B-\mu(\gamma_1+\gamma_2+\mu+\alpha))\cdot(\beta(\gamma_2(\eta+\mu+\alpha)+\eta\gamma_1) -\delta\gamma_2(\gamma_1+\gamma_2+\mu+\alpha))}{\beta\mu\left\{\begin{array}{l}\beta(\mu(\gamma_1+\gamma_2+\mu+2\alpha+\eta)+\alpha(\gamma_1+\gamma_2+\eta+\alpha)\\ +\eta(\gamma_1+\gamma_2))-\delta(\mu(\gamma_1+2\gamma_2+\mu+2\alpha)+\alpha(2\gamma_2+\alpha)\\ +\gamma_1(1+\gamma_2))\end{array}\right\}}$$

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 $E_1=(S,0,D_I,R)$ 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

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

$$trace(J) = \beta\frac{B}{\mu}+\delta\frac{B}{\mu}-\gamma_1-\gamma_2-2\alpha-4\mu<0$$

Therefore, E_0 is locally stable.

At point $E_1=(S,0,D_I,R)$, the Jacobean matrix takes the form,

$$J_1 = \begin{bmatrix} \left(\frac{-\delta B+\mu(\eta+\mu+\alpha)}{(\eta+\mu+\alpha)}\right)-\mu & -\beta\left(\frac{\eta+\mu+\alpha}{\delta}\right) & -\delta\left(\frac{\eta+\mu+\alpha}{\delta}\right) & 0 \\ 0 & \beta\left(\frac{\eta+\mu+\alpha}{\delta}\right)-\gamma_1-\gamma_2-\mu-\alpha & 0 & 0 \\ \frac{\delta B-\mu(\eta+\mu+\alpha)}{(\eta+\mu+\alpha)} & \gamma_1 & 0 & 0 \\ 0 & \gamma_2 & \eta & -\mu \end{bmatrix}$$

$$trace(J) = \frac{-\delta B+\mu(\eta+\mu+\alpha)}{(\eta+\mu+\alpha)}+\frac{\beta(\eta+\mu+\alpha)}{\delta}-\gamma_1-\gamma_2-\alpha-3\mu<0$$

Therefore, E_1 is locally stable.

Theorem 2. The unique positive equilibrium point E^* is locally asymptotically stable with the condition that $X_3>0$ if and only if $\beta(\eta+\mu+\alpha)>\delta(\gamma_1+\gamma_2+\mu+\alpha)$.

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

$$J^* = \begin{bmatrix} -x_1 & -\beta S^* & -\delta S^* & 0 \\ \beta D_B^* & -x_2 & 0 & 0 \\ \delta D_I^* & \gamma_1 & -x_3 & 0 \\ 0 & \gamma_2 & \eta & -\mu \end{bmatrix}$$

where

$$x_1=\beta D_B^*+\delta D_I^*+\mu, x_2=\gamma_1+\gamma_2+\mu+\alpha-\beta S^*, x_3=\eta+\mu+\alpha-\delta S^*$$

The characteristic polynomial of the above Jacobean matrix is

$$\lambda^4+X_1\lambda^3+X_2\lambda^2+X_3\lambda+\mu(\gamma_1\beta D_B^*\delta S^*+\delta^2 D_I^* S^* x_2+x_3\beta D_B^*\beta S^*+x_1x_2x_3)$$

Where

$$X_1=\mu+x_1+x_2+x_3$$

$$X_2=\mu(x_1+x_2+x_3)+\delta^2 D_I^* S^*+x_2x_3+x_1x_3+\beta^2 D_B^* S^*+x_1x_2$$

$$X_3=\mu(\delta^2 D_I^* S^*+\beta^2 D_B^* S^*+x_2x_3+x_1x_3+x_1x_2)+(\gamma_1\delta+\beta)\beta D_B^* S^* +\delta^2 D_I^* S^* x_2+x_1x_2x_3$$

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

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.

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

$$=1-R_0$$
$$=1-0.4660$$
$$=0.534>0$$

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 global asymptotically stable.

Proof: Consider, the Lyapunov function for $E_1=(S,0,D_I,R)$

$$L(t)=S(t)+D_B(t)+D_I(t)$$

$$L'(t)=S'(t)+D_B'(t)+D_I'(t)$$

$$=B-\mu S-\gamma_2 D_B-(\mu+\alpha)D_B-\eta D_I-(\mu+\alpha)D_I$$

$$\le B-\mu\left(\frac{B}{\mu}\right)-(\gamma_2 D_B+\eta D_I+(\mu+\alpha)D_B+(\mu+\alpha)D_I)$$

$$=-(\gamma_2 D_B+\eta D_I+(\mu+\alpha)D_B+(\mu+\alpha)D_I)$$

$$\le 0$$

Hence, E_1 is globally stable.

Consider, the Lyapunov function for $E^* = (S^*, D_B^*, D_I^*, R^*)$

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

$$L'(t) = \left[\left(S - S^*\right) + (D_B - D_B^*) + (D_I - D_I^*) + (R - R^*)\right]\left[S' + D_B' + D_B' + R'\right]$$

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

$$= \left\{\begin{array}{l} -\mu\left[\left(S - S^*\right) + (D_B - D_B^*) + (D_I - D_I^*) + (R - R^*)\right]^2 \\ -\alpha\left[(D_B - D_B^*) + (D_I - D_I^*)\right]\left[\left(S - S^*\right) + (D_B - D_B^*) + (D_I - D_I^*) + (R - R^*)\right] \end{array}\right\}$$

$$\leq 0$$

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)

$$V_\theta^{R_0} = \frac{\partial R_0}{\partial \theta} \cdot \frac{\theta}{R_0}$$

TABLE 2

SENSITIVITY ANALYSIS

Parameters	Sign	Interpretation
B	+	Prone to be diabetic if maternal history speaks of diabetes.
β	+	High level of glucose and insufficient production of insulin results diabetes.
γ_1 / γ_2	-	More diabetic individuals need to opt for dialysis at same of time.
η	0	No effect
δ	+	For severe diabetic individual only alternative is dialysis
μ	-	More individuals take prevention
α	-	Death is not related to diabetes or dialysis

, where θ denotes model parameters.

5 NUMERICAL SIMULATION

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

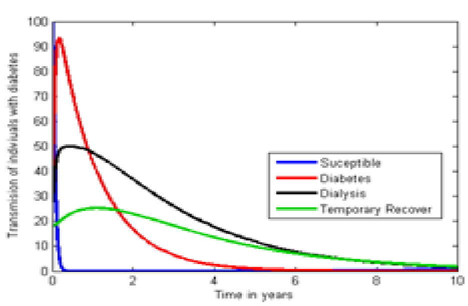

Fig. 2. Movement of each compartments

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.

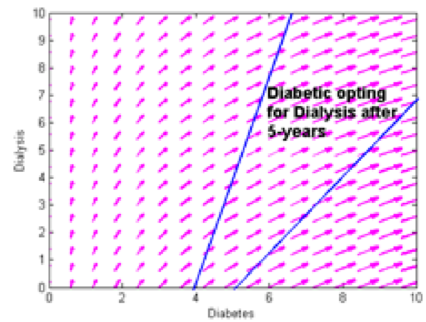

Fig. 3. Directed graph

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

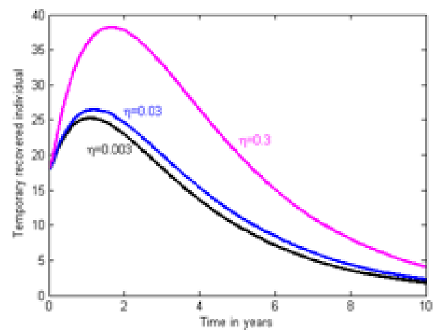

Fig. 4. Effect of η on R

Figure 4 shows the effect of the rate of individuals moving to temporary recovery class due to dialysis (η). 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.

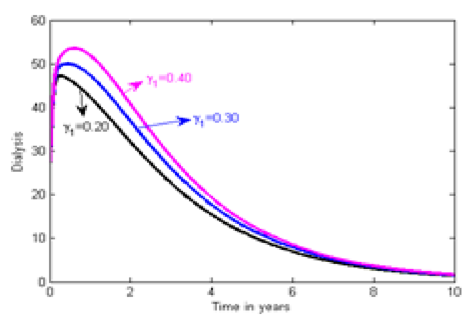

Fig. 5. Effect of γ_1 on D_I

Figure 5 shows that if the rate of individuals from diabetes to dialysis (γ_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.

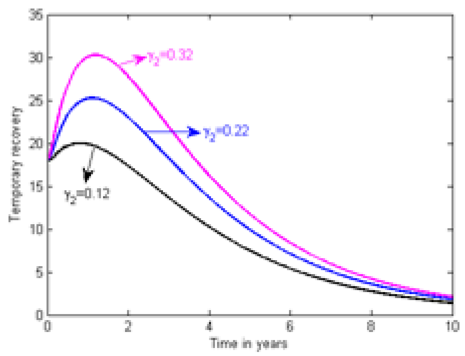

Fig. 6. Effect of γ_2 on R

Figure 6 shows that if the rate of individuals from diabetes to temporary recover (γ_2) 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 life style changes can lower the risk of sugar problem. To prevent diabetes, manage your weight, exercise regularly, eat a balanced healthy diet, reduce intake 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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8 REFERENCES

[1]. Boutayeb, E. H. Twizell K. Achouayb and A. Chetouani, “A mathematical model for the burden of diabetes and its complications”, BioMedical Engineering OnLine, vol. 3, no. 1, pp. 1-8, Jun 2004, doi:10.1186/1475-925X-3-20.

[2]. O. Diekmann, J. A. P. Heesterbeek and M. G. Roberts, “The construction of next-generation matrices for compartmental epidemic models”, Journal of the Royal Society Interface, vol. 7, pp. 873-885, Nov 2009, doi:10.1098/rsif.2009.0386.

[3]. P. G. Fabietti, V. Canonico, M. O. Federici, M. M. Benedetti and E. Sarti, “Control oriented model of insulin and glucose dynamics in type 1 diabetics”, Medical and Biological Engineering and Computing, vol. 44, no. 1-2, pp. 69-78, doi:10.1007/s11517-005-0012-2.

[4]. http://www.who.int/mediacentre/factsheets/fs355/en/

[5]. https://en.wikipedia.org/wiki/Disease

[6]. https://www.diabetes.co.uk/

[7]. https://www.medicalnewstoday.com/articles/152902.php

[8]. https://www.medicinenet.com/dialysis/article.htm

[9]. N. H. Shah, M. H. Satia and B. M. Yeolekar, “Optimum control for Spread of pollutants through Forest Resources”, Applied Mathematics, vol. 8, no. 5, pp. 607-620, 2017.

[10]. N. H. Shah, F. A. Thakkar and B. M. Yeolekar, “Dynamics of parking habits with punishment: An application of SEIR model”, Journal of Basic and Applied Research International, vol. 19, no. 3, pp. 168-174, 2016.