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A Mathematical Model for the Effects of Physical Activity and Nutrition in Patients with Diabetes Mellitus

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Abstract:

The disease of diabetes is ravaging the world's population affecting the lives of many people mainly the economically active groups. Its effects result in a decrease of the most productive world's labor force and consequently reducing the Gross Domestic Product (GDP). The objective of this study was to develop a mathematical model for Blood Glucose Regulatory System (BGRS) using Linear Nonhomogeneous Differential Equations. This model incorporated nutrition and physical activity, to be able to manage Diabetes mellitus in such a way that, the peak, which is the time period for insulin to be most effective in lowering blood sugar, is within the acceptable range. It is worth noting that after doing physical activity for some minutes, we have that the glucose and insulin levels in the blood plasma of diabetic patient decreases back to their normal levels. This means that if a patient observes the correct diet and does physical activity regularly and mostly once per day for a certain period, there is no need of going for any insulin supplement. This is more beneficial because the body may become resistant to introduction of insulin with time.

Keywords: Diabetes mellitus, external rates, physical activity, nutrition, stability

1. Introduction

Diabetes mellitus is a chronic condition in which blood glucose is above or below the normal range that is 3.5-10.0 mmol/L. The blood always has some glucose in it because the body needs glucose for energy and the glucose comes from the food we eat. When glucose builds up in the blood instead of going into cells, it can lead to *Diabetes mellitus*, [1]. The pancreas produces the hormone insulin that helps glucose get from the blood into body cells where it is converted into energy. In patients with *Diabetes mellitus*, the pancreas produces little or no insulin or body cells cannot respond to insulin very well. Glucose therefore cannot get into the cells and builds up in the blood. There are two main types of Diabetes. Type 1 *Diabetes mellitus* is hereditary and usually occurs in children or young adults accounting for about 5 to 10 % of all cases of *Diabetes mellitus*. Type 2 *Diabetes mellitus* is the most commonly occurring type of Diabetes; this form of *Diabetes mellitus* usually occurs in adults but is becoming more common in children and adolescents. In Type 2 *Diabetes mellitus*, the body is able to produce insulin but the insulin produced is either insufficient or the body is unable to respond to its effects which leads to a buildup of glucose in the blood. People with Type 2 *Diabetes mellitus* often need to take tablets or insulin to help the body's supply of insulin work better, [2]. *Diabetes Mellitus*, commonly known as diabetes is a syndrome of disordered metabolism, usually due to a combination of hereditary and environmental causes, resulting in abnormally high blood sugar levels known as hyperglycemia. During digestion, carbohydrates are broken down mainly into a simple sugar called glucose. When glucose enters the bloodstream, the pancreas goes into red alert. It secretes insulin into the blood, then the liver and muscles immediately remove glucose from the blood, when it fails to do so then diabetes occurs. *Diabetes mellitus* are classified into many types and this classification is based on the classification of the group of disorders which constitute the disease, that is, it is based on the pathogenesis of the disease though one of the most acceptable methods of classification of this disease is based on the verification method [5]. Despite uncountable campaigns, management and control strategies currently in place to achieve diabetes free world, *Diabetes mellitus* still remains one of the major chronic diseases in the world. Diabetes can cause skin problems, such as infections, sores, and itching. Skin problems are sometimes a first sign that someone has diabetes. Diabetes can lead to problems with teeth and gums, called gingivitis and periodontitis [12]. Lifestyle and environmental factors are reported to be the main causes of extreme increase in the incidence of Type 2 *Diabetes mellitus* [9]. Carbohydrates intake has a direct effect on postprandial glucose levels in people with diabetes and is the principal macronutrient of worry in glycemic management. In addition, an individual's food choices and energy balance have an effect on body weight, blood pressure and lipid levels directly

[10]. Physical activity positively contributes to overall health and well-being, [11]. Some of the studies did earlier include Li *et al* [7]; modeling the glucose insulin regulatory system and ultradian insulin secretory oscillations with two time delays. Kwach *et al* [6] developed and solved an extension of the model by Ackerman *et al*, taking into account epinephrine as a third variable, which lies in its ability to help in conducting a reliable test for detecting diabetes in the blood. These authors and other previous researchers did not take into consideration external rates such as nutrition and physical activity; hence this model ensured that physical activity and nutrition are being considered. This study therefore incorporated external rates which lie in their ability to keep the blood glucose level and cholesterol in target ranges, so that the peak, which is the time period for insulin to be most effective in lowering blood sugar, within a shorter time is in the acceptable therapeutic range. Bantle J.P *et al* [3] observing another delayed effect, namely the hepatic glucose production, in the glucose insulin regulatory system of normal people, based on the model proposed by [8] for normal glucose insulin regulatory system, H. Wang *et al* proposed the model to simulate the dynamics of the insulin therapies for type 1 diabetic patients. The two major factors in the regulatory system model are glucose and insulin, denoting $G(t)$ and $I(t)$ as glucose and insulin concentration at time $t = 0$, respectively. $I_{in}(t)$ represents the exogenous insulin infusion rate. The term $G_{in}(t)$ is glucose intake rate. The other source of glucose production is the liver. When the plasma glucose concentration level drops, α -cells, also located in the islets of Langerhans in the pancreas start to release another hormone, glucagon. Glucagon exerts control over pivotal metabolic path-ways in the liver and leads the liver to dispense glucose. Denghmingliani *et al* [4] proposed a mathematical model to study the impact of physical exercises on glycemic regulation. They performed linear, nonlinear and numerical analysis of glycemic regulation and they also applied the simulating modeling program 'Model Maker' for modeling. On introducing two external periodical functions defining diet and physical exercise in normal and diabetic cases, their numerical analysis showed that their model reflects glycemia and insulin dynamics of a healthy person and a diabetic person rather exactly. On comparing received numerical solutions of these models with experimental data, a fairly good coincidence of the models and the data was received and this fact allows applying the investigated model in monitoring complex systems. The above authors and other previous researchers did not take into consideration the rate at which physical activity and nutrition is being increased, which lies in their ability to keep the blood glucose level and cholesterol in target ranges, facilitates the healing process and finally prevents or delay diabetic problem so that when insulin is administered, it takes the minimum time possible to lower blood sugar.

2. Methodology

2.1. Methods of Solution

The stability of the model has been approached from Jacobian matrix method for checking stability of the disease and numerical simulations have been done using PYTHON to validate the analytic results.

2.2. Model Equations

The physical activity and nutrition on Diabetic model state equations are given by,

Figure 1: External Rates in a two Compartments Model

$$\begin{aligned} g'(t) &= -(k_1 + k_3)g(t) + k_4h(t) + p(t) \\ h'(t) &= k_3g(t) - (k_2 + k_4)h(t) \end{aligned} \quad (1)$$

Where

$g(t)$: Represent the glucose available in the blood plasma.

$h(t)$: Represents the insulin available in the blood plasma

$P(t)$: External source of glucose into the blood plasma. $p_1(t) + p_2(t)$.

$p_1(t)$: Rate of physical activity that trigger the level of glucose in the blood plasma.

$p_2(t)$: Amount of food substance entering the blood plasma

k_1 : Rate of glucose assimilation into the skeletal muscle tissues.

k_2 : Rate at which insulin is assimilated into the body cells.

k_3 : Rate at which excess glucose is converted to glycogen for storage.

k_4 : Rate of conversion of stored glycogen to glucose for uptake by skeletal muscle tissues

The model equation (1) can be written in matrix form,

$$X(t) = \begin{pmatrix} g \\ h \end{pmatrix}, \quad (2)$$

Where the coefficient matrix is given in the form;

$$\text{Where } A = \begin{pmatrix} -(k_1 + k_3) & k_4 \\ k_3 & -(k_2 + k_4) \end{pmatrix} \text{ and } B = p(t) \quad (3)$$

$$\text{where } P(t) = p_1(t) + p_2(t)$$

Which is

$$X'(t) = \begin{pmatrix} -(k_1 + k_3) & k_4 \\ k_3 & -(k_2 + k_4) \end{pmatrix} X(t) + \begin{pmatrix} p(t) \\ 0 \end{pmatrix} \quad (4)$$

$$\text{Where } A = \begin{pmatrix} -(k_1 + k_3) & k_4 \\ k_3 & -(k_2 + k_4) \end{pmatrix} \text{ which is the Jacobian matrix and } B(t) = \begin{pmatrix} p(t) \\ 0 \end{pmatrix}$$

$$\text{where } P(t) = p_1(t) + p_2(t)$$

Therefore, the equilibrium points are given by,

$$-(k_1 + k_3)g(t) + k_4h(t) + p(t) = 0 \quad \dots\dots(i)$$

$$k_3g(t) - (k_2 + k_4)h(t) = 0 \quad \dots\dots(ii) \quad (5)$$

From (5) we have,

$$g(t) = \frac{k_2 + k_4}{k_3} h(t) \quad (6)$$

Whereby eqn (6) comes from eqn (5, ii).

and substituting (6) into (5, i) we get that,

$$p(t) + k_4h(t) - \frac{(k_1 + k_3)(k_2 + k_4)}{k_3} h(t) = 0 \quad (7)$$

Multiplying both sides by k_3 and regrouping $h(t)$ we have,

$$h(t) = \frac{k_3 p(t)}{(k_1 + k_3)(k_2 + k_4) - k_4 k_3} = \frac{k_3 p(t)}{k_1 k_2 + k_1 k_4 + k_2 k_3} \quad (8)$$

Therefore, the equilibrium points are;

2.3. Equilibrium Points and Stability Analysis

$$g(t): \frac{(k_2 + k_4)p(t)}{k_1 k_2 + k_1 k_4 + k_2 k_3}, \quad h(t): \frac{k_3 p(t)}{k_1 k_2 + k_1 k_4 + k_2 k_3} \quad (9)$$

To check on stability

Unstable: Most solutions blow up as $t \rightarrow \infty$: the real part of some root is positive.

Stable: All solutions decay to zero as $t \rightarrow \infty$: the real parts of all roots are negative.

In the 2×2 case, we can work this out.

If $\det A < 0$, the roots must be real and of opposite sign: unstable.

If $\det A > 0$ and the roots are real, they must be either both positive

($\text{tr} A > 0$: unstable) or both negative ($\text{tr} A < 0$: stable).

If $\det A > 0$ and the roots are not real, then then $\text{Re} \lambda = \frac{\text{tr} A}{2}$

But again

$\text{tr} A > 0$: unstable; $\text{tr} A < 0$: stable.

To get the eigenvalues of A, we use the characteristics polynomial of the form;

$$p(\lambda) = \lambda^2 - \text{tr} A + \det A = 0 \quad (10)$$

The trace of matrix A is given as $\text{tr} A = -(k_1 + k_2 + k_3 + k_4) < 0$ and the determinant of A is given as;

$$\det A = (k_1 + k_3)(k_2 + k_4) - k_3 k_4.$$

$$= k_1 k_2 + k_1 k_4 + k_2 k_3 > 0$$

$$(11)$$

Therefore, the two eigenvalues of the Jacobian matrix A are;

$$\lambda_1 = \frac{\text{tr} A + \sqrt{(\text{tr} A)^2 - 4\det A}}{2} < 0, \text{ and } \lambda_2 = \frac{\text{tr} A - \sqrt{(\text{tr} A)^2 - 4\det A}}{2} < 0,$$

Therefore, we have $\text{tr} A = \lambda_1 + \lambda_2 < 0$ and $\det A = \lambda_1 \lambda_2 - k_3 k_4 > 0$, which implies that $\lambda_1 < 0$ and $\lambda_2 < 0$. This implies that the system of equations (1) is asymptotically stable.

The solution of (1) is;

$$X(t) = e^{tA}X_0 + \int_0^t e^{(t-z)A}B(z)dz \quad (12)$$

$e^{tA} = Pe^{tD}P^{-1}$, Where D is the diagonal matrix and P is the matrix of eigenvectors

3. Results and Discussion

This section comprises of parameter values obtained from secondary data and graphs obtained using PYTHON. The parameters are estimated by fitting the data below in python using the Least squares estimation Method. The least square estimation is used in this study since it is assumed that there are no errors involved in data collection. This is the data for glucose plasma levels during Frequently Sampled Intravenous Glucose Tolerance (FSIVGT) tests.

Time(mins)	Glucose(mg/dl)	Insulin(μ /ml)	Time(mins)	Glucose(mg/dl)	Insulin(μ /ml)
0	92	11	32	142	22
2	350	26	42	124	22
4	287	136	52	105	15
6	251	85	62	92	15
8	240	51	72	84	11
10	216	49	82	77	10
12	211	45	92	82	8
14	205	41	102	81	11
16	196	35	122	82	7
19	192	30	142	82	8
22	172	30	162	85	8
27	163	27	182	90	7

Table 1: Data for Glucose Plasma Levels during FSIVGT

For clearly illustrative purposes, secondary values of insulin and glucose plasma levels during Frequently Sampled Intravenous Glucose Tolerance (FSIVGT) test as shown in table(1) was used to show the effects of external rates when incorporated so that ,the time period for insulin to be most effective is in the acceptable therapeutic range[6].

Figure 2: The Effects of External Rates on the Levels of Glucose and Insulin for $T = 5$.

We can see that the glucose level in the blood plasma as high as 350 units and the level of insulin was high as 50 units at $t=0$ minutes. After doing the physical activity for only 5 minutes, we can see that the glucose in the blood plasma has reduced by almost 100 units and has also lowered the level of insulin in the blood plasma.

Figure 3: The Effects of External Rates on the Levels of Glucose and Insulin for $T=60$

After doing some physical activity, the glucose in the blood plasma has decreased to less than 100 units and insulin level in the blood plasma also has decreased to very low levels which are less than 20 units. This is the same case when $t=60$ mins. The glucose level goes below 50 units and it seems to be getting to its normal level. Insulin has also dropped to very low level since the body does not produce much of it to aid in absorption of glucose by the skeletal muscle tissues.

In figures 4, 5 and 6 after doing physical activity for 100 and 200 minutes, we have that the glucose and insulin levels in the blood plasma of diabetic patient decreases back to their normal levels as from 80th minute which they remain constant. This is the same case when $t=1000$ mins. This means that if a patient observes the correct diet and does physical activity regularly and mostly once per day for one and a half hours, there is no need of going for any insulin supplement. Therefore, if this continues, the body will be able to regulate the amount of sugar in the blood and insulin level in the body will be enough to control the normal glucose in the blood plasma. By doing this, diabetic patients will be able to fight this disease in a natural way and avoid taking many medications (insulin supplement). This is more beneficial because introduction of insulin to the body may become resistant with time. Physical activity and observation of the nutrition, is much better for everyone because it does not require more money compared to insulin supplement.

Figure 4: The Effects of External Rates on Levels of Glucose and Insulin for $T=100$

Figure 5: The Effects of External Rates on Levels of Glucose and Insulin for $T=200$

Figure 6: The Effects of External Rates on Levels of Glucose and Insulin for $T=1000$

4. Conclusion

The main objective was to formulate a mathematical model for BGRS, which incorporate external rates using First Order Liner Nonhomogeneous Differential Equations. The model is expressed as a system of linear nonhomogeneous equations in the form $Y' = AY + \tilde{r}(t)$. The effects of physical activity and nutrition are analyzed analytically and numerically using PYTHON. After doing some physical activity and observing the correct diet for a certain period of time. The blood plasma decreases and the insulin level in the blood plasma also decrease to very low levels. This means that if a patient observes the correct diet and does physical activity regularly and mostly once per day, there is no need of going for any insulin supplement. Therefore, if this continues, the body will be able to regulate the amount of sugar in the blood and insulin level in the body will be enough to control the normal glucose in the blood plasma. This is more beneficial because the body may become resistant to introduction of insulin with time.

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