Research Paper

Mathematical Model for the Dynamics of Glucose Regulatory System under the Combined Effect of Dieting and Physical Activity

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Abstract: *In this work, we present a mathematical model for the dynamics of glucose regulatory system under the combined use of dieting and physical activity, the model is an improvement on the work by Brian et al (2000). In our proposed model, we incorporated a parameter **h** by defining it in terms of; physical activity and dieting (calorie restriction) as factors that affects glucose and insulin homeostasis. The study ushered in a mathematical model for studying the dynamics of the glucose regulation under the combined effect of dieting (calorie restriction) and physical activity. The model was used to investigate the effect of dieting and physical activity on glucose and insulin homeostasis, The result of the study showed that; dieting and physical activity has great impact on the regulation of plasma glucose and insulin concentration, and that dieting and physical activity can be used on any population for the management of glucose and insulin homeostasis. Furthermore, our study corroborates the clinical trial studies by Margarita et al (2005), Jean (1999), that; dieting and physical activity improves insulin and glucose effectiveness on a wider scope rather than on a specific population as required by clinical trial studies. In conclusion, 1) Medical practitioners should encourage a combined physical activity and calorie restriction therapy for the management of diabetes, 2) Government, NGO's, and stake holders should improve on investment in physical activity facilities and production of low calorie diet for diabetic patients. Such therapy will attenuate the development of diabetes and transition from diabetes without complications to diabetes with complications in a diabetic population.*

1.0 Introduction

It is commonly admitted that diabetes is mainly encourage by decreasing levels of activity and increasing prevalence of obesity (Bouteyab*et al,* 2004). Weight control through dieting (*caloric restriction*) has been strongly recommended by medical practitioners. However, dieting fails to yield the desired impact at some point in time in the course of daily lives (*particularly for a diabetic patient*), and hence caloric restriction alone will not produce long-term weight loss, (Microsoft ® Encarta ®, 2009). Brian *et al* (2000) developed a mathematical model for β-cell mass, insulin and glucose dynamics, by consideringβ-cell mass, plasma insulin concentrations, and plasma glucose concentrationsas the primary variables of the glucose regulatory system. Their model (*which they used instudying the behavior of the glucose regulatory system and pathways to diabetes*) was presented as:

$$\frac{dG}{dt} = R_0 - (E_{GO} + S_I I)G$$

$$\frac{dI}{dt} = \frac{\beta\sigma G^2}{\alpha + G^2} - KI$$

$$\frac{d\beta}{dt} = (-d_0 + r_1 G - r_2 G^2)\beta$$

Where;

R_0 = is the net rate of glucose production at zero glucose level

E_{GO} = is the total glucose effectiveness at zero insulin level

S_I = is the total insulin sensitivity

β= Beta cell mass

G= Blood glucose concentration

σ= Rate of insulin secretion by the pancreatic beta cells

I= Blood insulin concentration

K, a, r_1, r_2 are constants

d_0 = Beta cell death rate at zero glucose level

(For the normal values of the above parameters see table I, appendix A)

Derouich and Boutayeb (2002), used a modified version of the minimal model to introduced parameters related to physical exercise (Boutayeb and Chetouani, 2006). The modified version of the minimal model by Derouich and Bouteyab, 2002,is given as:

$$\frac{dG}{dt} = -(1 + q_2)X(t)G(t) + (p_1 + q_1)(G_0 - G(t))$$

$$\frac{dX(t)}{dt} = -p_2X(t) + (p_3 + q_3) + (I(t) - I_b)$$

Where q_1, q_2, q_3 parameters are related to physical activity and are defined as follows:

q_1:   The effect of physical exercise in accelerating the utilization of glucose by muscles and the liver.

q_2:   The effect of physical exercise in increasing the muscular and liver sensitivity to theaction of insulin.

q_3:   The effect of physical exercise in increasing the utilization of insulin. In other words, q_3 increases insulin effectiveness in enhancing glucose disposal and consequently improving insulin sensitivity.

In this work we propose the extension of the work by Brian *et al* (2000) by incorporating dieting and physical activity as other factors that affects plasma glucose and insulin kinetics. The factors considered and defined in this work are; i) *Plasma glucose level (concentration) denoted by G, ii) Plasma insulin level (concentration) denoted by I, iii) Beta cell mass denoted by β iv) physical exercise level (amount of calories burnt through physical exercise) denoted by EX and dieting(calorie restriction) denoted by d.*

2.0 Methodology

2.0.1 Assumptions

❖   Glucose concentration change is not rapid
❖   Extreme physiological and chemically induced trauma is excluded so that the rate of neogenesis and transdifferentiation will be negligible.

2.0.2 Notations

R_0 =   is the net rate of glucose production at zero glucose level

E_{GO} =   is the total glucose effectiveness at zero insulin level

S_I =   is the total insulin sensitivity

β   =   Beta cell mass

G   =   Blood glucose concentration

σ   =   Rate of insulin secretion by the pancreatic beta cells

I   =   Blood insulin concentration

K, a, r_1, r_2=   are constants

d_0 =   Beta cell death rate at zero glucose level

d   =   Denotes the level of dieting in terms of calorie intake

EX   =   The amount calories burnt as a result of physical exercise

| h | $=\frac{EX}{d}$ | dieting andphysicalexercise effectiveness in accelerating theutilization of glucoseby muscles and the liver. |

| q_1 | = | effect of physical exercise and dieting in accelerating the utilizationofglucose by muscles and the liver. |

| q_2 | = | effect of physical exercise and dieting in increasing the utilization ofinsulin |

2.0.3 Model Building

In developing the mathematical equations for the dynamics of the glucose regulatory system that incorporates dieting and physical exercise through a control parameter, we defined and introduced the parameter denoted by*h* as a ratio of physical activity (*amount of calories burnt through exercise*) denoted by EX, and dieting (*amount of calorie intake*) denoted by *d.*

2.0.3.1 Glucose Dynamics

➢ **Glucose Production:**

In a normal glucose regulatory system, glucose production is regulated as follows:

- At zero (0) glucose level, a steady glucose production rate of P_0 is maintained for all plasma insulin levels.
- For a given non-zero plasma glucose level & a steady plasma insulin level, glucose production decreases linearly with respect to glucose levels.

$$\Rightarrow glu\cos e\ production \propto G = -\chi G$$

Hence glucose $production = P_0 - \chi G$ (Brian *et. al*, 2000), Brian *et.al* (2000)estimated the constant χ as the sum of:

- Glucose effectiveness for production at zero insulin level = E_{GOP}
- Insulin effectiveness for production at the steady insulin level I = S_{IP} I

$$\therefore \chi = E_{GOP} + S_{IP}I$$
$$\Rightarrow production = P_0 - (E_{GOP} + S_{IP}I)G$$

In this work, we maintain the above expression for glucose production

➢ **Glucose Uptake:**

In a normal glucose regulatory system, glucose uptake is regulated as follows:

- At zero plasma glucose level a steady glucose uptake rate U_0 is maintained for all plasma insulin levels.
- For a given non zero plasma glucose level and a steady plasma insulin level, glucose uptake increases linearly with respect to glucose level.

$$\Rightarrow glu\cos e\ uptake \propto G = K_1 G$$

Hence glucose uptake = $U_0 + K_1 G$ (Brian *et al,* 2000).

Brian *et al,* 2000, estimated the constant K_1 as the sum of:

i)   Glucose effectiveness for uptake at zero insulin level = E_{GOU}
ii)   Insulin effectiveness for uptake at the steady insulin level I = S_{IU} I

$$\therefore K_1 = E_{GOU} + S_{IU} I$$

In this work, we redefined K_1 by incorporating the effect of physical exercise and dieting in accelerating the utilization of glucose by muscles and the liver, denoted by q_1. Thus our new K_1 will be estimated as the sum of:

-       Glucose effectiveness for uptake at zero insulin level = E_{GOU}
-       Insulin effectiveness for uptake at the steady insulin level I = S_{IU} I
-       The effect of physical exercise and dieting in accelerating the utilization of glucose by muscles and the liver, q_1.

$$\therefore K_1 = E_{GOU} + S_{IU} I + q_1$$
$$\Rightarrow uptake = U_0 + \left(E_{GOU} + S_{IU} I + q_1 \right) G$$

Thus, the equation governing glucose dynamics based on the single-compartment approach by *(Brian et al, 2000), adopted from Bergman et al, 1985*) is given as;

$$\frac{dG}{dt} = production - Uptake$$
$$= P_0 - \left(E_{GOP} + S_{IP} I \right) G - U_0 - \left(E_{GOU} + S_{IU} I + q_1 \right) G$$
$$= (P_0 - U_0) - \left[\left(E_{GOP} + E_{GOU} \right) + \left(S_{IP} I + S_{IU} I + q_1 \right) \right] G = R_0 - \left(E_{GO} + S_I I + q_1 \right) G$$
$$\Rightarrow \frac{dG}{dt} = R_0 - \left(E_{GO} + S_I I + q_1 \right) G$$

Where $R_0 = P_0 - U_0$, $E_{GO} = E_{GOP} + E_{GOU}$, $S_I = S_{IP} + S_{IU}$

2.0.3.2 Insulin Dynamics

➢   **Insulin Clearance:**

Brian *et al*, 2000 gave the insulin clearance expression as:

Insulin clearance = KI

Where K is a clearance constant, representing the combined insulin uptake at the liver, kidney and insulin receptors.

In this work, we redefine K by incorporating the effect of physical exercise and dieting in influencing the utilization of insulin, denoted by q_2. Thus our new K represents the combined sum of:

-       Insulin uptake at the liver, kidney and insulin receptor, δ.
-       Insulin uptake as a result of physical exercise and dieting, q_2 .s

Thus; *our new* K= δ + q_2, and the insulin clearance expression = $(δ + q_2)$I

> **Insulin Secretion:**

Net insulin secretion rate can be modeled as a sigmoidal function of glucose level (Brian *et al*, 2000). This exposition is backed by (Cobelli *et al, 1980 &* Rudenski *et al,* 1991) who successfully used sigmoidal insulin secretion rates. The relative contributions of β-cell recruitment and cellular insulin secretion have not been quantified functionally, but the rate of secretion from individual β-cells varies with glucose (Salomon and Meda, 1986). On the basis of this, Brian *et al* (2000) gave the net insulin secretion rate as a sigmoidal function of glucose level as;

$$Insulin \ \sec retion = \frac{\beta \sigma G^2}{(\alpha + G^2)}$$

Where α is a constant and $\frac{\beta \sigma G^2}{(\alpha + G^2)} \subseteq [0,1]$ is a hill function that describes the sigmoid.

In this work, we maintain the above expression for insulin secretion.

Thus, the equation governing insulin dynamics (based on the single-compartment approach by Brian et al, 2000, adopted from Bergman et al, 1985) is given by;

$$\frac{dI}{dt} = Secreation - Clearance \equiv \frac{dI}{dt} = \frac{\beta \sigma G^2}{\alpha + G^2} - (\delta + q_2)I$$

2.0.3.3 β-Cell Mass Dynamics

> **β-cell Replication:**

Brian *et al* (2000), reported that; In vitro studies by Swenne (1982), Hugl *et al* (1998), showed that the percentage of β-cells undergoing replication varies as a non-linear function of glucose level in the medium, and replication rates for β-cells increases with increasing glucose levels; however, at extreme hyperglycemia, β-cell replication may be reduced, whence Brian *et al*(2000) modeled this behavior with a simple 2nd degree polynomial as:

$$Replication \ = (r_{1r}G - r_{2r}G^2)\beta ----------------(A)$$

Where r_{1r} *(measured in $mg^{-1} dl \ day^{-1}$) and* r_{2r} *(measured in $mg^{-2} dl^2 \ day^{-1}$)* are rate constants. In this work, we also maintain the above expression for β-cell replication

> **β-cell Loss:**

Brian *et al* (2000) reported that; In vitro studies by Hoorens*et al* (1996), Efanova*et al* (1998), showed that β-celldeathvaries non-linearly with glucoselevel changes, whence Brian *et al*(2000), modeled β-celldeathwith a simple 2nd degree polynomial as:

$$Death = (d_0 - r_{1a}G + r_{2a}G^2)\beta --------------------(B)$$

Where d_0 *(measured in d^{-1}) is the death rate at zero glu$\cos e$ and* r_{1a} *(measured in $mg \ dl \ d^{-1}$)*
& r_{2a} *(measured in $mg \ dl \ d^{-1}$) are cons$\tan ts$.*

Brian *et al* (2000) gave the equation for β-cell dynamics (*based on the single-compartment approach by* Brian *et al* (*2000*), *adopted from* Bergman *et al* (*1985*)), as;

$$\frac{d\beta}{dt} = Formation - Loss$$

$$\frac{d\beta}{dt} = (-d_0 + r_1 G - r_2 G^2)\beta; \quad Where\ r_1 = r_{1r} + r_{1a}\ ,\quad r_2 = r_{2r} + r_{2a} \quad \text{are constants}$$

We also maintain the above expression for β-cell death for this work.

2.0.4 Estimating q_1 & q_2

Body glucose deteriorates with physical activity(Encarta, 2009), and high carbohydrate/low fat deteriorate insulin sensitivity (Jean, *1999*). Hence q_1 and q_2, can be estimated as follows:

$q_1 \propto \frac{EX}{d} \equiv q_1 = E_{GO}\frac{EX}{d};$ *Where E_{GO} is the glucose effectiveness*

$q_2 \propto \frac{EX}{d} \equiv q_2 = S_I\frac{EX}{d};$ *Where S_I is the insulin sensitivity*

Hence our complete model system of equations that describes glucose, insulin and β-cell dynamics incorporating physical exercise and dieting is as follows;

$$\left.\begin{aligned}\frac{dG}{dt} &= R_0 - (E_{GO} + S_I I + q_1)G \\[2mm] \frac{dI}{dt} &= \frac{\beta\sigma G^2}{\alpha + G^2} - (\delta + q_2)I \\[2mm] \frac{d\beta}{dt} &= (-d_0 + r_1 G - r_2 G^2)\beta\end{aligned}\right\} - - - - - - - - - - - - - -(1)$$

With $q_1 = E_{GO}\frac{EX}{d}, and\ q_2 = S_I\frac{EX}{d}$

2.0.5 Analysis

We study the equilibrium solution of the system bysplitting the glucose regulatory system into; Fast (*Glucose and Insulin*) subsystem, and slow (*β-cell*) subsystemas follows;

➢   **Fast(Glucose and Insulin) Subsystem**

The null clines of the first two equationsof system (1) (*equations of the glucose and insulin subsystem*)are;

i) $\dfrac{dG}{dt} = R_0 - (E_{GO} + S_I I + q_1)G = 0 \Rightarrow G = \dfrac{R_0}{E_{GO} + S_I I + q_1}$ - - - - - -(2)

ii) $\dfrac{dI}{dt} = \dfrac{\beta\sigma G^2}{\alpha + G^2} - (\delta + q_2)I = 0 \Rightarrow I = \dfrac{\beta\sigma G^2}{\left(\alpha + G^2\right)(\delta + q_2)}$ - - - - - - -(3)

Now, we study (*hypothetically)* the effect of dietary restrictions and physical activity on plasma glucose and insulin concentrations using the above null clines, to this effect, a computer program was developed to simulate the null cline equations. The data generated from the program using the null cline equations (2) and (3) was used to plot the following **Fig.1** and **Fig.2** respectively
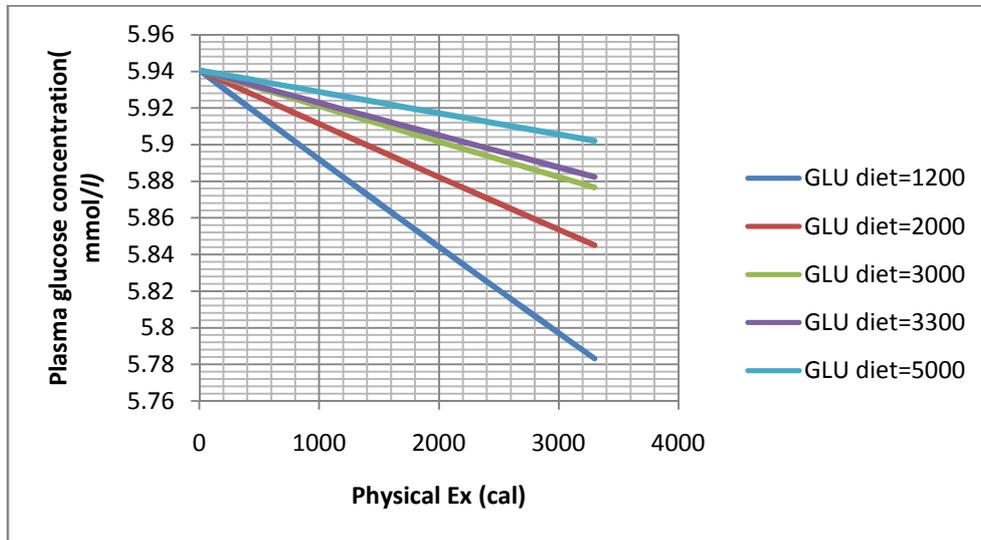

Fig 1: Effect of varying dietary restrictions and physical activity on plasma glucose concentration ("Gludiet" represents glucose concentration under "x" calorielevel of dieting)
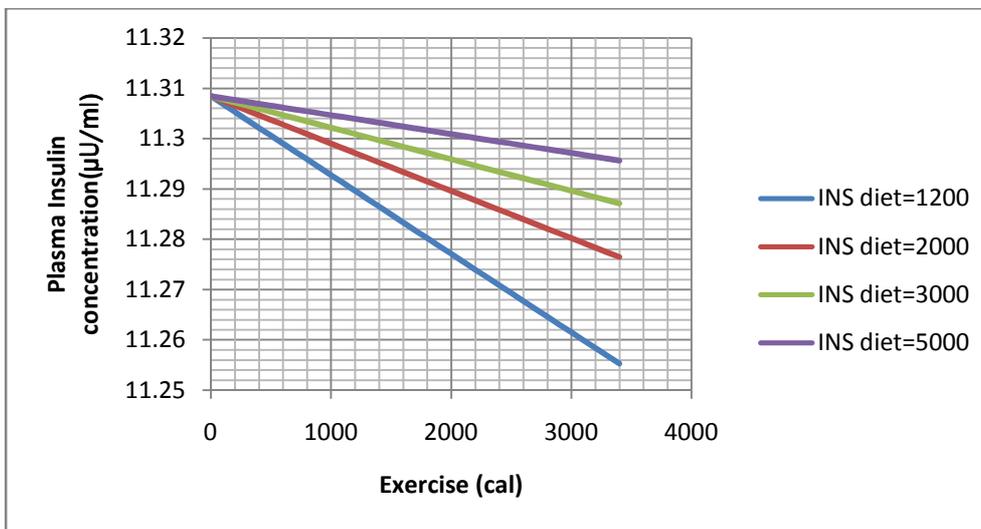

Fig 2: Effect of varying dietary restrictions and physical activity on plasma insulin concentration ("INS diet" representsInsulin concentration under "x" calorielevel of dieting)

➢ **Slow (β-cell)Subsystem**

The null cline of the equation of this subsystem is as follows;

i) $\quad \dfrac{d\beta}{dt} = (-d_0 + r_1 G - r_2 G^2)\beta = 0 \Rightarrow - d_0 + r_1 G - r_2 G^2 = 0$ or $\beta = 0$

Substituting the values of the parameters from **table 1** appendix A, we have;

$$600000 - 8400G + 24G^2 = 0, or \, \beta = 0$$

$$This \Rightarrow G = \frac{8400 \mp \sqrt{12960000}}{48} or \, \beta = 0$$

$\therefore G = 100 \, or \, 250 \, and \beta = 0 \, are the optimal (steadysate) \, values for the \beta - cells \, dynamics$

$$\therefore \frac{d\beta}{dt} = 0 \text{ when } G = 100 \, or \, 250 \, or \, \beta = 0$$

To understand the meaning of these optimal points, we need to draw the graph of β-cell death & replication (*Equations B & A respectively*) as follows;
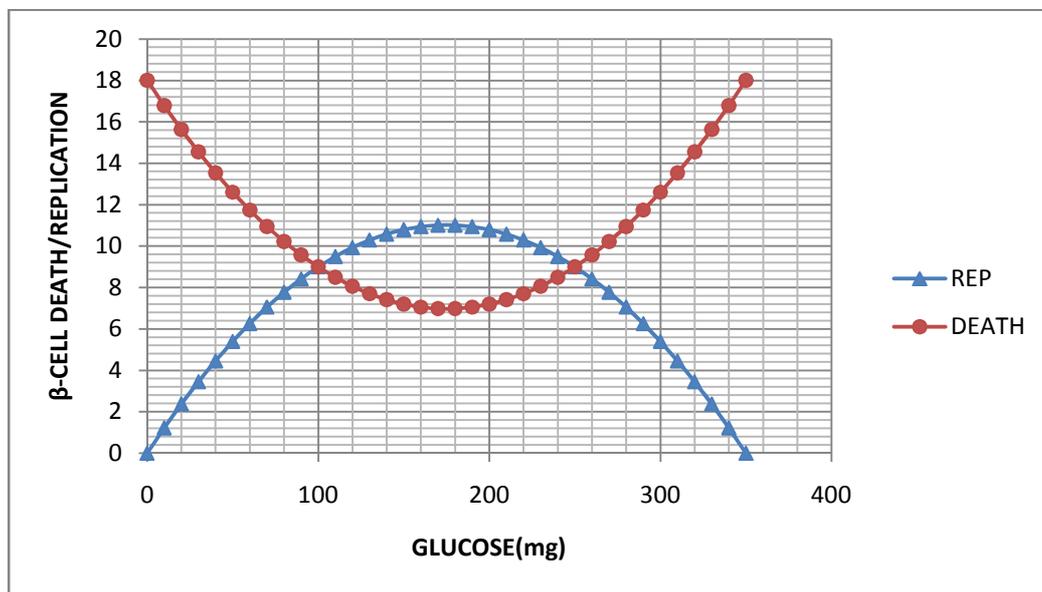

Figure 3: Shows the relationship between the dynamics of beta cell death and replication

3.0 Results and Discussion

In this work, we have developed a mathematical model for the study of the dynamics of the glucose regulatory system under the combine effect of dieting and physical activity, the model consist of system of differential equations that describes glucose, insulin and β-cell dynamics incorporating physical activity and dieting. The comprehensive model is given as follows;

$$\left. \begin{array}{l} \dfrac{dG}{dt} = R_0 - (E_{GO} + S_I I + q_1)G \\[2mm] \dfrac{dI}{dt} = \dfrac{\beta \sigma G^2}{\alpha + G^2} - (\delta + q_2)I \\[2mm] \dfrac{d\beta}{dt} = (-d_0 + r_1 G - r_2 G^2)\beta \end{array} \right\} - - - - - - - - - - - - - (1)$$

With $q_1 = E_{GO} \frac{EX}{d}, and q_2 = S_I \frac{EX}{d}$

We discussed our result under subheadings as follows;

3.0.1 Glucose Regulation

Looking at the null cline equation (2) $G = \dfrac{R_0}{E_{GO} + S_I I + q_1}$, we have;

$$\lim_{S_I \to 0} G = \lim_{S_I \to 0} \left(\frac{R_0}{E_{GO} + S_I I + q_1} \right) = \left(\frac{R_0}{E_{GO} + q_1} \right)$$

Thus as insulin sensitivity S_I deteriorates, glucose is regulated by glucose effectiveness E_{GO}, dietary restriction *d*, and physical activity, EX. This analytical results of ours corroborates the clinical trial results of Margarita *et al* (2005), and jean *et al* (1999) that; dieting and physical activity improves insulin and glucose effectiveness, and regulate gene expression. Since type II diabetes is characterized by Insulin resistance by cells,this study suggests that dietary restriction, and physical activity is a good therapy for type II diabetes.

Looking at the nullcline equation (3)we, have;

$$\lim_{\beta \to 0} I = \lim_{\beta \to 0} \left(\frac{\beta \sigma G^2}{(\alpha + G^2)(\delta + q_2)} \right) = 0$$

Thus, as β-cell mass deteriorates, so also insulin production by the pancreas deteriorates, However, Teran-Garcia, *et al*(2005), Margarita *et al*(2005), jean *et al*(1999), have demonstrated the efficacy of physical exercise, they showed that; physical activity regulates gene expression, hence β-cell replication will be stimulated through gene expression. Since type I diabetes is characterized by inadequate insulin production by the pancreas as a result of low β-cell mass in the pancreas due to autoimmune destruction ofβ-cells, physical exercise will help in improving β-cell mass, thus regulating glucose.In this case, there is the need for exogenous insulin for survival to be followed by dietary restriction *d* and improve physical activity EX to take advantage of the control parameter$q_2 = S_I \frac{EX}{d}$ to regulate gene expression. This is in line with current medical practice for type I diabetes management.

From **fig.1**, it can be seen that, as physical exercise (*Burnt calorie*) increases, plasma glucose decreases faster at low calorie intakes. This is as a result of improvement in glucose uptake and utilization in body.

From **fig.2,** it can be seen that as physical exercise (*Burnt calorie*) increases, plasma insulin concentration decreases faster at low calorie intakes. This is as a result of improvement in insulin uptake effectiveness in the body.

Fig.3 depicts the global behavior of the slow subsystem which shows the points where the β-cell replication and β-cell death curves intersect at glucose levels of G=100 and 250. This isnon-trivial steady states as pointed out by Brian *et al* (2000). Brian *et al* (2000) called this points; physiological fixed point (P) and a saddle point (S) respectively, they further partitioned the plot plane into; zone I (area before the 1st intersection, zone II (area between the intersections) and zone III (area after the second intersection). Brian et al (2000) explained further that In Zone I, death rates exceed replication rates, driving β-cell mass down and causing the steady-state glucose level to rise. In Zone II, replication rates exceed death rates, driving β-cell mass up and the blood glucose level down. Zones I

and II constitute a basin of attraction for the physiological fixed point (P). In Zone III, death exceeds replication, causing a decrease in β-cell mass, thus driving the glucose level even higher. This is a zone of pathological regulation, in which the system is driven to the trivial steady state of zero β-cell mass.

3.0.1.1 Gradients of the Glucose Dynamics under Dieting and Physical Activity Graphs

Looking at **fig. 1**, we have;

i)   Gradient of graph @ 1200cal dietary level and varying level of physical exercise isestimated by: (5.844-5.82)/(2500-2000)=0.008/500=**0.000048**

ii)   Gradient of graph @ 2000cal dietary level and varying levels of physical exercise isestimated by:(5.896-5.868)/(2500-1500)=0.028/1000=**0.000028**

iii)   Gradient of graph @ 3000cal dietary level and varying level of physical exercise isestimated by:(5.92-5.88)/(3100-1000)=0.04/1000=**0.000019**

iv)   Gradient of graph @ 3300cal dietary level and varying level of physical exercise isestimated by:(5.924-5.896)/(2500-700)=0.028/1800=**0.000016**

v)   Gradient of graph @ 5000cal dietary level and varying level of physical activity isestimated by(5.92-5.912)/(2400-1700)=0.008/700=**0.000011**

Thus, it can be seen that; with decreasing calorie intake augmented with increase in physical exercise, the level of descend (*gradient*) of the glucose dynamics graphs increases, such that the lower the calorie intake and higher physical exercise, the higher the descent. This shows that;

> As physical exercise (*Burnt calorie*) increases, plasma glucose levelsdecreases faster with low calorie intake. This may be as a result of improvement in glucose uptake and utilization in the body due to increase in physical activity and calorie restriction.

3.0.1.2 Gradients of the Insulin Dynamics under Dieting and Physical Activity Graphs

Looking at **fig 2**, we have;

i)   Gradient of graph @1200cal dietary level and varying level of physical exercise isestimated by:(11.308-11.28)/(1800-0)=0.028/1800=**0.000016**

ii)   Gradient of graph @ 2000cal dietary level and varying level of physical exercise is estimated by:(11.294-11.28)/(3000-1500)=0.014/1500=**0.0000093**

iii)   Gradient of graph @ 3000cal dietary level and varying level of physical exercise is estimated by:(11.296-11.29)/(2900-1900)=0.06/1000=**0.000006**

iv)   Gradient of graph @ 3300cal dietary level and varying level of physical exercise is estimated by:(11.3-11.29)/(3200-1500)=0.01/1700=**0.0000059**

v)   Gradient of graph @ 5000cal dietary level and varying level of physical exercise is estimated by:(11.3-11.296)/(3300-2600)=0.004/700=**0.0000057**

Thus, it can be seen that; with decreasing calorie intake augmented with increase in physical exercise, the level of descend (*gradient*) of the insulin dynamics graphs increases, such that the lower the calorie intake and higher physical exercise, the higher the descent. This shows that;

> As physical exercise (*Burnt calorie*) increases, plasma insulin levels decreases faster with low calorie intake. This may be as a result of improvement in insulin uptake in the body due to increase in physical activity and calorie restriction.

Thus, results 3.0.1.1&3.0.1.2 suggest that; controlled dieting and physical exercise reduces plasma glucose and insulin levels, hence physical exercise and dieting can be used to regulate plasma glucose and insulin levels.

This study has analytically demonstrated that;

1)   Physical exercise and dieting reduces plasma glucose levels.
2)   Physical exercise and dieting improves insulin sensitivity by reducing the amount of insulin required to improve glucose uptake.

We summarized that;

> Combining our analytical results with the result by Teran-Garcia, *et al*(2005), Margarita *et al*(2005), jean *et al*(1999), we deduce that; plasma glucose levels, insulin sensitivity and hence diabetes can controlled throughcombined physical activity and dietary restriction therapy.

4.0 Conclusion

In this work, we developed mathematical model equations that described the glucose regulatory system under the combined use of dieting and physical exercise. We were able to show, through the model, that: Sustained physical activity and dieting is sure way to regulate plasma glucose and insulin concentrations. This will attenuate the rate developing complications as a result of diabetes. Also, the model was used to study defects in Insulin sensitivity deterioration, and β-cell mass deterioration on the glucose regulatory system under the influence of dieting and physical activity, where it was shown that, for type I diabetes, physical exercise has very negligible effect in improving plasma glucose disposal when β-cell mass deteriorates, hence the need for an exogenous insulin therapy for survival. Whereas for type II diabetes, it was shown that physical exercise alone (*with insulin sensitivity>>0*) can be used to improve glucose disposal, and thus enhancing plasma glucose regulation. In the event where insulin sensitivity≈0, Physical exercise which improves insulin effectiveness can improve glucose disposal, and thus enhancing plasma glucose regulation. We therefore recommend as follows;

1)   Medical practitioners should encourage a combined physical activity and calorie restriction therapy for the management of diabetes.
2)   Government, NGO's, and stake holders should improve on investment in physical activity facilities and production of low calorie diet for diabetic patients.

Appendix A

Parameter	Value	Units
S_I	0.72	$ml\mu U^{-1}d^{-1}$
E_{GO}	1.44	d^{-1}
R_o	864	$mlgd l^{-1}d^{-1}$

σ	43.2	$\mu U m l^{-1} d^{-1}$
α	20000	$mg^2 d l^{-2}$
K	432	d^{-1}
d_o	0.06	d^{-1}
r_1	0.84×10^{-3}	$mg^{-1} d l d^{-1}$
r_2	0.24×10^{-5}	$mg^{-2} d l^2 d^{-1}$

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