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Modelling the Re-Growth of Beta Cells in Autoimmune Diabetes

Okorie, Charity Ebelechukwu[1*], Ogwumu, David Onah[2], Nwaokolo Martin Afam[3]

[1,2,3]*Department of Mathematics and Statistics, Federal University, Wukari, Taraba State, Nigeria.*

*okoriec636@gmail.com

Abstract - Type 1 diabetes is a type of disease that occurs when the beta cells that produce insulin are killed by the T cells. Diabetes has been a serious menace in the whole world. It has killed and deformed many people all over the world. Science has made it possible that there are a lot of varieties of drugs for the treatment of diabetes. Despite all these, many people still have diabetes. Many are finding it difficult to manage their diabetes. Despite the access diabetes has gained in technology which makes instruments for testing diabetes available, yet many people do not carry out this test to ascertain their status. Also, those who have access to the equipment are not even kin for the treatment of diabetes, which has contributed to some complications. In this research work, we modified a model proposed by Mahaffy and Edelstein Keshet (2007). In their model, we observed that they did not consider re-growth of dead beta cells. In our model, we introduce a parameter (g) (which will take care of the dead beta cells by way of re-growth to prevent diabetes from getting to the stage of complication. We validated our model by carrying out simulations with the parameter (g). The results obtained showed that the moment the re-growth parameter is introduced, Beta cells, which have a value of 0.00 at the initial time, begin to increase to 4.89, and the T cells decrease to 3.12 at 20 % of the re-growing parameter. At 50%, beta cells increased to 10.3 while T cells decreased to 3.08. At 70% of the regenerating parameter, beta cells increased to 16.16 while T cells decreased to 3.08. At 90%, beta cells increased to 25.98, and T cells decreased to 2.98. This study shows that the introduction of the re-growth parameter creates hope for diabetic patients.

Keywords - Re-growth parameter, Diabetic patients, Type 1 diabetes, Simulation, Insulin.

1. Introduction

Diabetes mellitus (or diabetes) is derived from the Greek word *diabetes*, meaning siphon - to pass through and the Latin word *mellitus*, meaning honeyed or sweet. This is because, in diabetes, excess sugar is found in the blood as well as the urine. It was known in the 17th century as the "pissing evil". The term diabetes was probably coined by Apollonius of Memphis around 250 BC (Das and Siddhartha, 2011). Diabetes was first recorded in English, in the form of diabetes, in a medical text written around 1425 (Das and Siddhartha, 2011). It was in 1675 that Thomas Willis added the word "'mellitus'" to the word diabetes (Das and Siddhartha, 2011). Diabetes mellitus is a metabolic disorder with characteristics of hyperglycaemia and insufficiency of secretion or action of endogenous insulin (American Diabetes Association, 2010). Family history is a known risk factor for type 1 diabetes. Other risk factors can include having certain infections or diseases of the pancreas (American Diabetes Association (ADA)) (2012). Diabetes Mellitus (DM) is defined as a group of metabolic disorders exerting significant pressure on human health worldwide (Kavakiotiset al., 2017).

In our previous study, it was observed that the rate at which patients are diagnosed with diabetes has been on the increase despite the series of diabetic drugs that are available.

Inna et al. (2014) developed an Ordinary Differential Equations (ODE) model of the physiological regulation of glycemia in type 1 diabetes.

Sandhya and Kumar (2011) proposed a mathematical model for studying DM for regulating glucose insulin in the system. They took into account all plasma glucose concentrations, generalized insulin, and plasma insulin concentrations. Eiko (2015) recently studied the trends in blood glucose control. Mathematical models were introduced in modelling glucose-insulin metabolism, followed by some representative blood glucose control systems, where most of them use model predictive control as a control algorithm.

2. Research Methodology

We attempted to modify the existing model proposed by Mahaffy and Edelstein-Keshet (2007), cyclic waves of circulating T cells in autoimmune diabetes. We then proposed a model that will re-re-grow the beta cells that are killed by the circulating T cells in their model. This formulation is done by adding a re-growing parameter (g) to their model.

2.1. Model Equations of the Modified Model

$$\frac{dA}{dt} = (\sigma + \alpha M)f_1(p) - (\beta + \delta_A)A - \in A^2 \tag{1}$$

$$\frac{dM}{dt} = \beta 2^{m1}f_2(p)A - f_1(p)\alpha M - \delta_m M \tag{2}$$

$$\frac{dE}{dt} = \beta 2^{m2}(1 - f_2(p)A - \delta_\in E \tag{3}$$

$$\frac{dp}{dt} = REB - \delta_p p \tag{4}$$

$$\frac{dB}{dt} = -kEB + gEB \tag{5}$$

For the peptide-dependent functions, we take the Hill function

$$f_1(p) = \frac{p^n}{k_{1+}^n p^n} \tag{6}$$

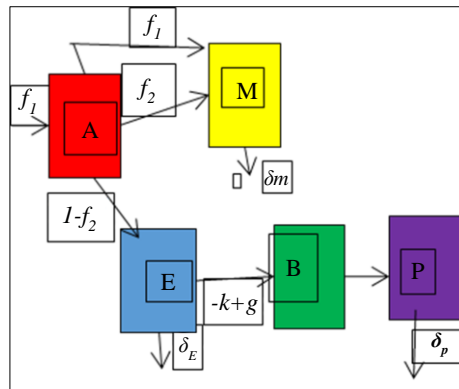$$f_2(p) = \frac{\alpha k_2^m}{k_2^m + p^m} \tag{7}$$

Fig. 1 The flow diagram of the modified Mahaffy and Edelstein-Keshet (2007)

2.2. Model Description and Formulation

We develop a system of ordinary differential equations with five compartments for autoimmune diabetes. The compartments comprise the activator, memory, effector, peptide and beta cell. As the extension of the existing model, we shall consider the regeneration parameter (g), which was not captured in the existing model.

2.3. Limitation and Modification on the Existing Autoimmune Diabetes Model of Mahaffy and Edelstein-Keshet (2007)

The model covers the attack of the T cells on the beta cells until the beta cells are gone, and the moment the beta cells are no more, diabetes sets in. The model did not address the regeneration of the beta cells that will help to control diabetes after it has set in. As a result, we incorporated a re-growing parameter g to account for the generation of beta cells that can help in the control of diabetes and prevent it from getting to the stage of complications.

2.4. Model Assumption of the Proposed/ Modified Autoimmune Diabetes

We assume that developed diabetes can be controlled as soon as the dead beta cells are replaced with a newly grown beta cell.

3. Results of the Analysis

Here, we compute the numerical solutions/ simulations on the modified model and then make recommendations. The results are shown in the figures and tables below;
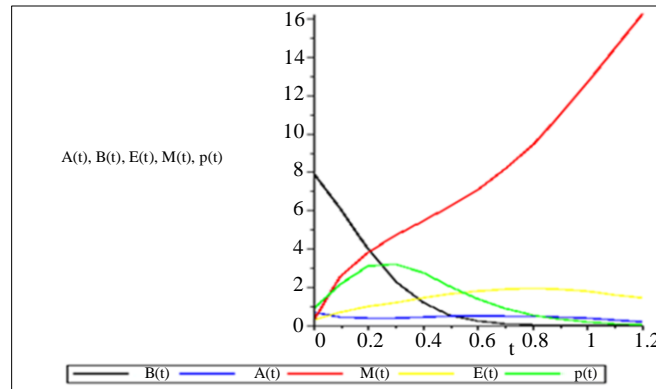

Fig. 2 The graph has no re-growing parameter

From the graph above, we discovered that Memory cells and effector cells are increasing, and the beta cells and peptides keep decreasing. This shows that if nothing is done to re-grow the beta cells, diabetic patients will likely have complications.
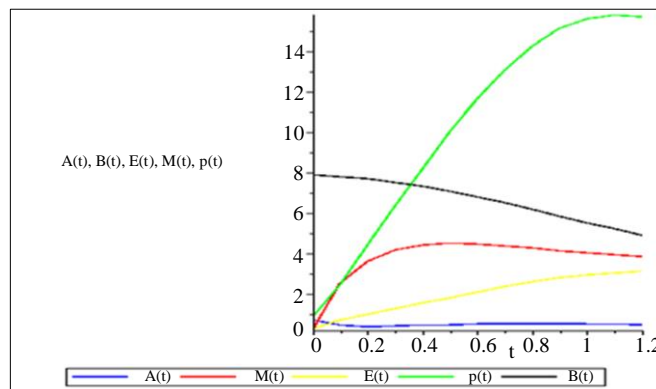

Fig. 3 The graph of the re-growing parameter introduced at 20%

At 20% introduction of beta cells regenerating parameter, the beta cells began to increase, while Activator, Memory and Effector cells started dropping.
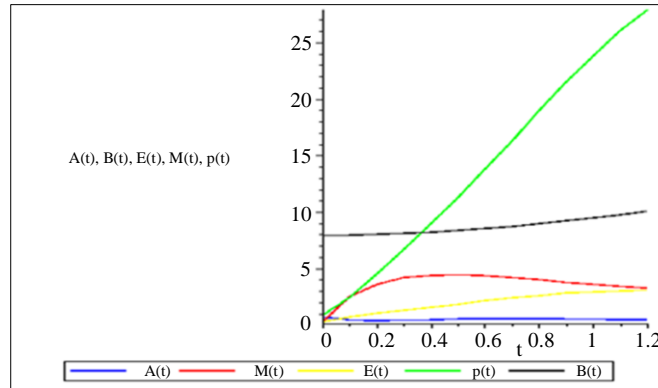

Fig. 4 The graph of the re-growing parameter introduced at 50%

From this graph, we discovered that at 50% re-growth of beta cells, Activator, Memory, and Effector cells kept decreasing, while Beta cells and peptides kept increasing.
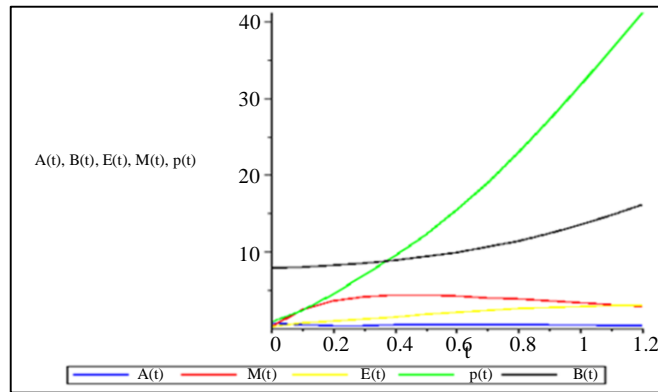

Fig. 5 The graph of the re-growing parameter introduced at 70%

The graph shows that at 70% of the re-growing parameter, the beta cells and peptide increase while the T cells decrease.
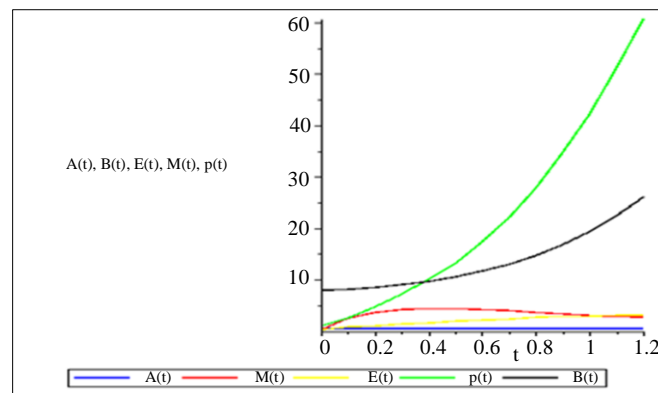

Fig. 6 The graph of the re-growing parameter introduced at 90%

From this graph, we discovered that the moment a re-generating parameter was introduced, the beta cells began to increase. At 90% introduction of re-growing parameters, the beta cell will increase rapidly while the memory and effector cells will drastically reduce. This shows that, at this point, once the beta cells start to produce insulin again, diabetic patients will not get to the stage of having complications.

Table 1. Initial value solution

Scale	B(t)	E(t)
0	7.90000000000000	0.285300000000000
0.10000000000000	6.10759809851001	0.709077115259338
0.20000000000000	3.98202627123356	0.987080655664697
0.30000000000000	2.29527134815605	1.21270274023952
0.40000000000000	1.18670406146442	1.42447547306719
0.50000000000000	0.553593911387357	1.62185417503627
0.60000000000000	0.235718220341885	1.78578264179028
0.70000000000000	0.093697793466931	1.89336370080619
0.80000000000000	0.0359292773255745	1.92769358595475
0.90000000000000	0.0138106038462298	1.88416339008364
1	0.0055228408785907	1.77193029386802
1.1000000000000	0.0023675364520302	1.60970090846234
1.2000000000000	0.0011095660188939	1.41867909145147

Table 1 shows that as T cells attack the beta cells and beta cells keep decreasing to the point of zero, where the insulin can no longer be produced. At this point, diabetes set in.

Table 2. The re-growing parameter is introduced at 20%

Scale	B(t)	E(t)
0	7.90000000000000	0.28530000000000
0.10000000000000	7.81893889278083	0.71288025995319
0.20000000000000	7.68456125301386	1.00860360512926
0.30000000000000	7.51137272317583	1.27027950316305
0.40000000000000	7.30340953539888	1.53978169285898
0.50000000000000	7.06216198033022	1.82012608625636
0.60000000000000	6.7907051741129	2.09764566966262
0.70000000000000	6.4946548491274	2.35634635804893
0.80000000000000	6.1811657056150	2.58434992738782
0.90000000000000	5.85821832349645	2.77537426519144
1	5.53310356438676	2.92796476846287
1.1000000000000	5.21203538345593	3.04409507241528
1.2000000000000	4.89983316510628	3.12784772369637

Table 2 shows the moment when the re-generating parameter is introduced; the beta cells begin to pick up as the T cells decline.

Table 3. At 50% of the re-growing parameter

Scale	B(t)	E(t)
0	7.900000000000	0.28530000000000
0.10000000000000	7.94085041058075	0.71312381861174
0.20000000000000	8.01003714109485	1.00997873783567
0.30000000000000	8.10204639722939	1.27381854582734
0.40000000000000	8.21699694646933	1.54626076655826
0.50000000000000	8.35683809448145	1.82965153320321
0.60000000000000	8.52314853688180	2.10938883296650
0.70000000000000	8.71633175584037	2.36845162124040
0.80000000000000	8.9359139903959	2.59395451803817
0.90000000000000	9.1792095690863	2.77867826445568
1	9.44187146439582	2.92031352050532
1.1000000000000	9.7293783153896	3.02006051281311
1.2000000000000	10.0316457457244	3.08131392063345

From Table 3, we discovered that at 50% introduction of the regenerating parameter. The beta cells increase to 10.03, while the T cells decrease to 3.08.

Table 4. At 70% of the re-growing parameter

Scale	B(t)	E(t)
0	7.90000000000000	0.28530000000000
0.10000000000000	8.23486121723711	0.71328657118506
0.20000000000000	8.23486121723711	1.01089700185691
0.30000000000000	8.52231301536716	1.27616923417335
0.40000000000000	8.89109798724355	1.55050981455619
0.50000000000000	9.35426744075724	1.83574461325773
0.60000000000000	9.92593893189516	2,11654898247183
0.70000000000000	10.6185405373684	2.37510837763280
0.80000000000000	11.4420698856632	2.59776213862699
0.90000000000000	12.4041026635414	2.77657822759729
1	13.5098976155794	2.90860860653039
1.1000000000000	14.7623728141013	2.99448836167181
1.2000000000000	16.1619378421831	3.03711464852777

Table 4 shows that the Beta cells increased to 16.16 at 70% of the re-growing parameter while the T cells decreased with 3.03.

Table 5. At 90% of the re-growing parameter

Scale	B(t)	E(t)
0	7.90000000000000	0.28530000000000
0.10000000000000	8.10641122462652	0.71344962745629
0.20000000000000	8.46617475030088	1.01181642230780
0.30000000000000	8.96513583761878	1.27851248486218
0.40000000000000	9.62256090771152	1.55470064027939
0.50000000000000	10.4751032892134	1.84162814372141
0.60000000000000	11.5673264282444	2.12317422775929
0.70000000000000	12.9476608876560	2.38066027103847
0.80000000000000	14.6670683232412	2.59960166957645
0.90000000000000	16.7782893917451	2.77133902645291
1	19.3344905467290	2.89231315467585
1.1000000000000	22.3868126625650	2.96266266510154
1.2000000000000	25.9807038799770	2.98488866519588

Table 5 shows that at 90% of the re-growing parameter, Beta cells increased to 25.98 while T cells will have a decrease of 2,98.

4. Conclusion

Diabetes is a disease that is not respectful of a person. This is so because it is a disease that can affect young, old, rich and even poor. Even though it has no permanent cure, it can also be managed if the patient can adhere to the things that can help in re-growing dead beta cells. This is so because, looking at the result of the analysis, we discovered that at the time when the re-generating parameter was not introduced, the beta cells declined to the extent of getting to zero. This is seen in Figure 2 and also in Table 1. Beta cells kept decreasing, from 7.9 in year 0 and 0.001 in the twelve years. When the re-growing parameter is introduced at 20% in Figure 3, we observed an increase in the beta cells while there was a decrease in the Effector cells. Also, the beta cells increased to 4.8 in the twelve years. In Figure 3 and Table 3, which is the introduction of a re-growing factor at 50%, Effector cells decreased, while beta cells experienced an increase at 10.03 in the twelve years against effector cells that decreased to 3.08. At 70%of the re-growth, the beta cells increased at 16.16 while T cells decreased at 3.03. In 90% of the re-generating parameter, beta cells increased at 25.98 while T cells decreased at 2.98.

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