Relevance of Glucose Level Variation Trend in Diabetic Patient's Blood and Onset of Diabetic Retinopathy Problems

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ABSTRACT

Majority of the world population is affected with diabetes. Retina of eye is found to involve in one third to one fourth of diabetics as a complication called diabetic retinopathy which is one of the most common causes of blindness in diabetes. It has been found that duration of diabetes with characteristic rise and fall is major cause for damage to retina. Various spans of remarkably elevated blood sugar levels often results into changes in perfusion of retinal capillaries bed which leads to onset of diabetic retinopathy. Many associated physiological dynamics have revealed the various modes of clustering of events affecting this condition. Computer simulation based methodologies have been used to solve various issues primarily related to bio-medical complications. Our effort in this work is to check the significant pattern of glucose level dynamics with some data trend responsible for causing diabetic retinopathy condition. The characteristic span profile of the dynamics is found to be held responsible for critical conditions. The obtained data set is trained meanwhile using neural network to predict the possibility of occurrence of such situation with relevant statistical inferences.

Keywords: Retina, Diabetic Retinopathy, Data Trend, Span Profile and Physiological Dynamics.

1. INTRODUCTION

Computational approaches are now being developed to resolve and predict the occurrence of several most common health disorders. Diabetes is a common physiological disease affecting a majority of world population. It is reported that diabetes mellitus affects 4 per cent of the world's population and about half of that have some sort of diabetic retinopathy problem at some stage [1]. Diabetic retinopathy is a common complication in diabetes and is a most prevalent cause of legal blindness between ages of 20 and 65 years. Diabetic retinopathy is more common in type I (insulin dependent or early onset) diabetes (in 40% cases) than in type II (non-insulin dependent or late onset) diabetes (in 20% cases). Such retinopathy occurs in type I as well as type II diabetes mellitus cases and it has also been found that most of type I and about three-fourth of type II sugar patients will develop retinopathy after one and half decade of their diabetic span [2]. Duration of diabetes is a more important risk factor than its metabolic control. In type I diabetics, retinopathy rarely develops within five years of onset of diabetes or before puberty, but 5% of type II diabetics have retinopathy at first presentation of diabetes. It is observed that very strict glycemic monitoring and control is required to cure surgical and cardiac patients, likewise precautions methodology are devised to avoid the occurrence of retinopathy problems [6,7]. Prolonged spans of elevated blood sugar levels often results into remarkable changes in perfusion of retinal blood capillaries with loss of pericytes and increased adhesiveness of blood cells and platelets in retinal vasculature of the eye leads to onset of diabetic retinopathy. Many associated physiological dynamics pertaining to anemia, protienurea, dyslipidemia and hypertention affect this condition.

The stipulation can be avoided to a certain extent by predicting the risk which arises only after sustenance or variation of blood sugar level in a characteristic way by using the data trend of a certain time span. The long term profile of glucose level can be used in computing the exact time of the approaching risk when the patient must get proper regulation of blood sugar level to avoid any significant damage to retina.

The modelling of time span profile for diabetic retinopathy is done in order to compute the exact time of falling into risk. The screening policies are also to be implemented for the early detection of retinopathy in patients with even non-insulin dependent diabetes [3]. The insulin dosage is carefully administered to diabetic patients with higher level of complications and on the other hand there are chances to develop retinopathy problems in meanwhile stage [4,5]. Using the profile one can go directly to consult his ophthalmologist in the initial stage of such a condition and need not wait for having complaints in the vision to make such a move. Model equations are found to be of great help in depicting and characterizing the dynamics and hence concluding some decisions based on numerical outcome of the putative model. The outcome of the model is iteratively being incorporated to the neural network and each numerical value is optimized using genetic algorithm to achieve more accuracy. It is found that neural network approach can be used for making predictions based on training given to the collected data. Each input data is first normalized and make to a certain scale then the values are trained, tested and validated to setup a neural network model. The temporal based massive data is available to support data mining research and working on models this effort is reasonably utilized in field of medical care [8].

The dynamics of other physiological factors are to be assimilated into the baseline sugar trend models in type I and type II diabetes to optimize the goal. Moreover statistical analysis has been made to identify the precise risk zone. Some co-incidental roles of indispensable genetic factors have been incorporated in the model to substantially develop a worthy approach. Although a lot of efforts workers did in characterizing diabetic retinopathy but a very inadequate noticeable work can be found which is dedicated particularly to resolve its cause. Digital chips based on this approach may be devised to monitor glucose level variation trends particularly for the patients falling in a defined risk zone. The accurate predictions based on these approaches would be of great help to identify the meticulous inception of such eye disorders.

2. A TYPICAL DIABETIC RETINOPATHY

Diabetic retinopathy is the most common diabetic disease of eye found to be a leading cause of blindness in most of the adult population. It is caused by adverse changes in the blood vessels of the retina. Generally in diabetic retinopathy, blood vessels may swell and leak fluid while in some cases abnormal new blood vessels grow on the surface of the retina, as shown in **Fig**. **(1)**, the retina is the light-sensitive tissue at the back of the eye required for vision. Diabetic retinopathy involve retina in five stages viz. mild, moderate, severe and very severe non-proliferative retinopathy and proliferative retinopathy. Former types (non-proliferative) are associated somehow with varying degree of obstruction in blood supply to retina while later stage (proliferative) is characterized by growth of new blood vessels with fragile wall along the interface of retina and vitreous i.e. neovascularisation. In such retinopathy the abnormal new blood vessels being fragile get damaged and result in blurring or loss of vision due to leaking of blood on macula or into vitreous cavity. The fluid and proteins may leak into the macula and its centre i.e. fovea where vision is sharpest, leading to blurring of vision. Such condition is defined as macular edema. It may usually occur at any stage of diabetic retinopathy but often tends to occur with the progress of disease. Most of the patients with proliferative retinopathy have macular edema.

To protect vision, every person including young and mature people with type I or II diabetes should have a comprehensive dilated eye examination as soon as possible after detection of diabetes and also get it done at regular intervals as required. Symptoms like floating spots are observed associated to haemorrhages that tend to happen more than once. If left untreated, proliferative retinopathy may result into severe vision loss and even total blindness.

Diabetic retinopathy characterized by macular edema is detected during a comprehensive eye tests as, visual acuity test, dilated eye exam, tonometry, fluorescein angiogram etc. To prevent progression of diabetic retinopathy effectively patient with diabetes is required to control his blood pressure, and blood cholesterol level additionally to blood sugar. Anaemia and nephropathy should also be investigated for and treated. Focal laser surgery is required for treating macular edema. Procedure called scatter laser treatment and surgical vitrectomy are quite effective in treating proliferative retinopathy. Now researchers are testing drugs that may have potential to stop retina from sending chemical signals (growth factors) to promote growth of new blood vessels. And also to block and render tem ineffective if released. These drugs might be of help in reducing the need for laser surgery to treat diabetic retinopathy problems.

Diabetic Retinopathy Condition

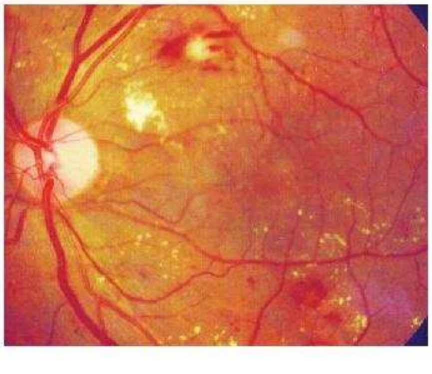

Figure 1. Perfusion of blood capillaries associated to diabetic retinopathy condition.

The clinical findings diagnosis at several stages over a vast time phase resulted into database for some numerical based study and risk characterization.

3. ROLE OF GLUCOSE LEVEL DYNAMICS

Glucose level dynamics is used to govern several physiological key factors and their interaction dynamics at each and every instance. In our study of diabetic retinopathy the impact of its higher level sustenance and frequent variable peaks are considered to be matter for prime research. The focus here is to allocate numerical weight factor that may incorporate several considerations included, at any point of time. The training of such data using neural network etc provide some clue in identifying the risk zone using statistical base and would become the matter of clinical attentiveness. Various other altered physiological states mentioned above like anemia, dyslipidemia, albuminurea and hypertention etc. along with genetic variants may interplay with glycemic status dynamics and if all could be computed may provide a vivid and continuous shade of expression in prediction of diabetic retinopathy.

Observed Glucose Dynamics at long term basis

Data of blood sugar level (fasting) has been assumed to configure a model framework which is used in critical study of its subjective dynamics. An observed data-set for a certain length of period has randomly selected to utilize for our putative model, **Table (1)**.

Blood Glucose level (mg/dL)	108.1	104.3	79.2	…	135.2	122.1
Time-Period (months)	1	2	3	…	69	70

Table 1. Observation time in months and recorded blood sugar level in mg/dL for respective duration

Utilizing the above data trend we would be able to utilize approach of data mining which have been generally used to apply over the population of data to screen out the data of interest in order to conduct a relevant statistical analysis.

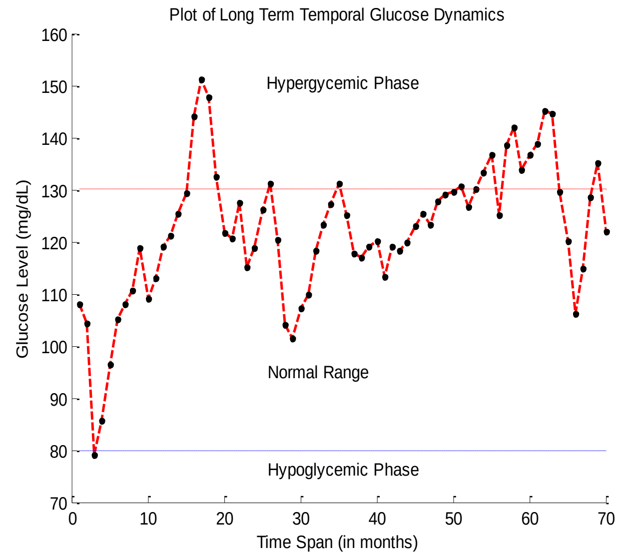

Figure 2. Observed trend of general variation in glucose level with selected time span in diabetes

4. ALGORITHM AND DATA ANALYSIS

To identify the Risk Prone Zone (RPZ) computationally from the entire observed data is the forth most task. Generally glucose level shows abrupt variations over a period of time in a diabetic patient **Fig. (2)**.

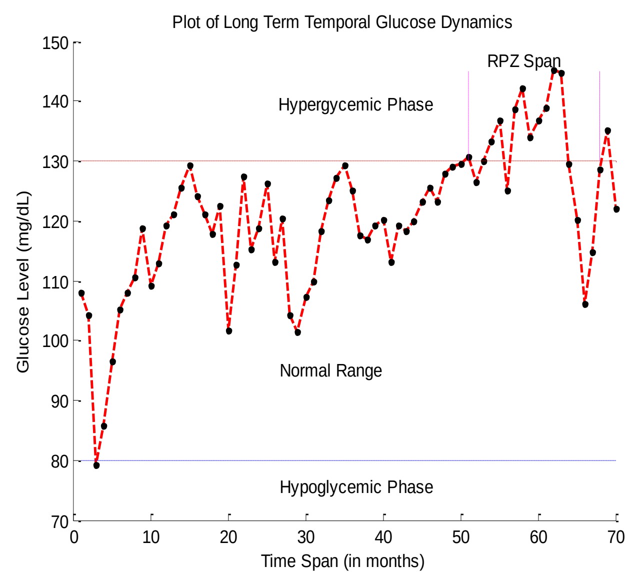

Figure 3. Identification of Risk Prone Zone from glucose level profile at certain period of span

Relevance of Statistical Analysis

According to the assumptions of our model the factors that are to be taken into account to compute the risk factor are;

- Span length of rise in blood sugar level above the normal
- Magnitude of different elevations in blood sugar during a particular span
- Frequency of such abnormal rise in any short duration of time length

Allocating weight to the above different parameters a simple model can be configured. We may compute risk factor variable (R_f) of diabetes to cause retinopathy at any point of time within any risk prone zone, shown **Fig. (3)**.

$$R_f = wgl_t * wt_i * X_{ps} \quad .....(1)$$

$$X_{ps} = Rs_t * Rf_{i-1} \quad .....(2)$$

i – Denotes the index for particular span; t – Time step

X_{ps} Weight of the previous high level glucose span

wgl_t Weight of the glucose level magnitude

wt_i Weight of the time factor or temporal issue

Rs_t Reliability value at a particular time instance

Rf_{i-1} The risk factor computed for previous span

In a risk prone zone span, depicted in **Eq. (1)** & **(2)** where parameter R_f follows a sigmoidal path while X_{ps} shows a decay with time based reliability factor (Rs_t) in between the different elevated sugar level spans. The other associated physiological factors governing glucose level and vision loss are not incorporated in overall study. Also the impact of treatment and dosage regulation not included separately to signify their role in shaping the data. The effort has been made just to incorporate the general data into the model to understand the vision related issue.

The first assumption envisages over the fact that any functional unit has initially maximum reliability and it decreases on basis of interaction of several subunits in a specific topological fashion with variable dynamics, **Fig. (4)**. A varying consequence of transformation in topology can be taken into account to depict the observed level of functionality at any point over a period of time. The general reliability term expression is considered here, **Eq. (3)**.

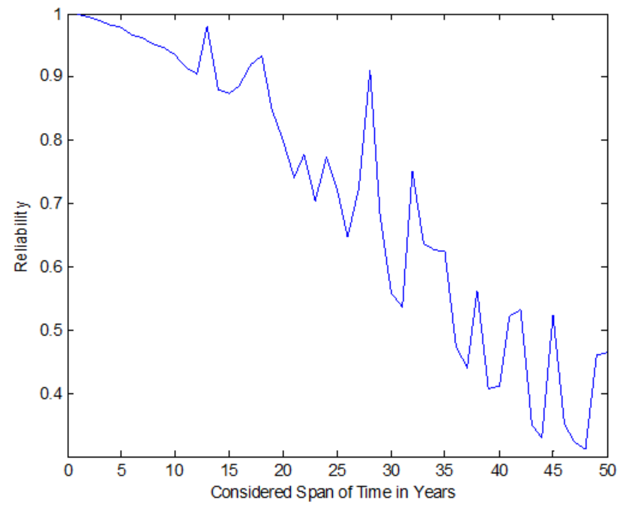

Figure 4. Stochastically decreasing reliability factor for visual system in diabetic situation.

Reliability at a time t is given by;

$$Rt = e^{-lambda * t} \quad .....(3)$$

The variable lambda – Denoted the chances of failure
e – Euler's number, having numerical value 2.7183

More effectively we can write for a an interactive small frame where two subunits are interacting sequentially while other three are also working in sequential harmony to each other, but the group of two and three are interacting in parallel fashion. The reliability of this small system with a small value for chance of failure (lambda of respective subunit i – lbdi) can be computed in respect to span of time, given by the equation **Eq. (4)**;

$$Rs(t) = e^{(-(lbd1 + lbd2) * t)} + e^{(-(lbd3 + lbd4 + lbd5) * t)} \quad .....(4)$$

It is preferable that large population size data has to be processed to design it for statistical test. Subsequently p-value is to be taken into account to signify the existence of risk zone over any band of time scale. Although reliability has very undersized impact over the biological system model but it always impart the property of decaying strength over time. So the strength of risk prone band has significant influence of this factor. Here stochastic assumption among functional subunits is made that may result into feasible functional outcome of any system as in our case visual framework.

Neural Network Applications

The simulation of glucose dynamics has been done in Matlab 8.0 to numerically evaluate and predict the process behaviour using neural network approach.

The data is first normalized using upper and lower bound of the numerical range and then the normalized data is used to serve as input for the neural network model. The procedure is repeated for train, test and validation data. Constituting the hidden layer a multilayer perceptron is designed to process the input together with weight. Using activation function as sigmoidal type the output is obtained. The given input is data set of sugar patient for entire observable time duration. After optimizing the number of layers to ensure optimal memory, ten hidden layers of neurons in the network are assumed. Inbuilt tool box is employed to build the neural network and to obtain the output of statistical significance.

The idea is to predict the Risk Prone Zone over the period of time from the given data, once it has been trained earlier with requisite data set. The model validation for a specific data profile is required to train and test the data after normalization, since each input data is first normalized and make to a certain scale then the values are trained, tested and validated to setup a neural network model. So adjusting the weight strength and minimizing the error more optimal predictions may be obtained regarding the temporal based inception of problems. Meanwhile data is optimized using genetic algorithm operation applying an objective function to ensure more optimized input data for neural network after its operation.

5. CONCLUSIONS

It was observed that span of glucose elevation in the blood is also important in addition to the level of glucose in the blood. So three things are collectively assumed to be relevant to reach any statistical conclusion i.e., times for which glucose level went high, magnitude of its elevation and span for which high frequency of glucose elevation or sustained increase in level is recorded. This strategy is to be applied over a long term observation which would give some inference of identifying the chances of onset of risk prone zone. It is also to be noticed that the study of physiological dynamics and its impact over retinopathy studied has still have to incorporate the significant influence of plenty of other factors and ailment conditions to make the approach more realistic and applicable.

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