HbA1c: A Study on Connectivity between Measurement of HbA1c and Hospital Readmission Rates

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Abstract: Hyperglycemia inpatient with diabetes mellitus (DM) is associated with high rate in mortality and morbidity. The aim of study is to obtain measurement of haemoglobin A1c and glucose insulin therapy is implemented to reduce the readmission rate and cost of individual treatment to evaluate the performance and usefulness of expert system, decision tree algorithm, regression method in reduction of readmission rate by HbA1c measurement in hyperglycemia inpatient. Logistic regression analysis used to compare patients with mean A1c<7% and with mean A1c>10% , mortality rate 4.6% .BG level prior to treatment of SSI and 70/30 insulin results in 204±68mg/dL and 200±50mg/dL respectively. HbA1c was performed by multivariable logistic regression is 18.4% in the inpatient setting. Statistical methods on primary diagnosis suggest the relationship between readmission rate and HbA1c of hyperglycemia inpatient with diabetes.

IndexTerms - HbA1c, SSI, DM, Hb, BBI, C4.5

I. Introduction

1.1 Overview of haemoglobin

The respiratory pigment found in red blood corpuscles is known as haemoglobin. It is conjugated protein. There are two components in haemoglobin namely Haem and Globin. Haem is combination of iron (Fe), a charged atom and 4% of porphyrin content. Globin is 96% of amino acids. Both these compound gives red color to the blood.

1.2 Haemoglobin structure

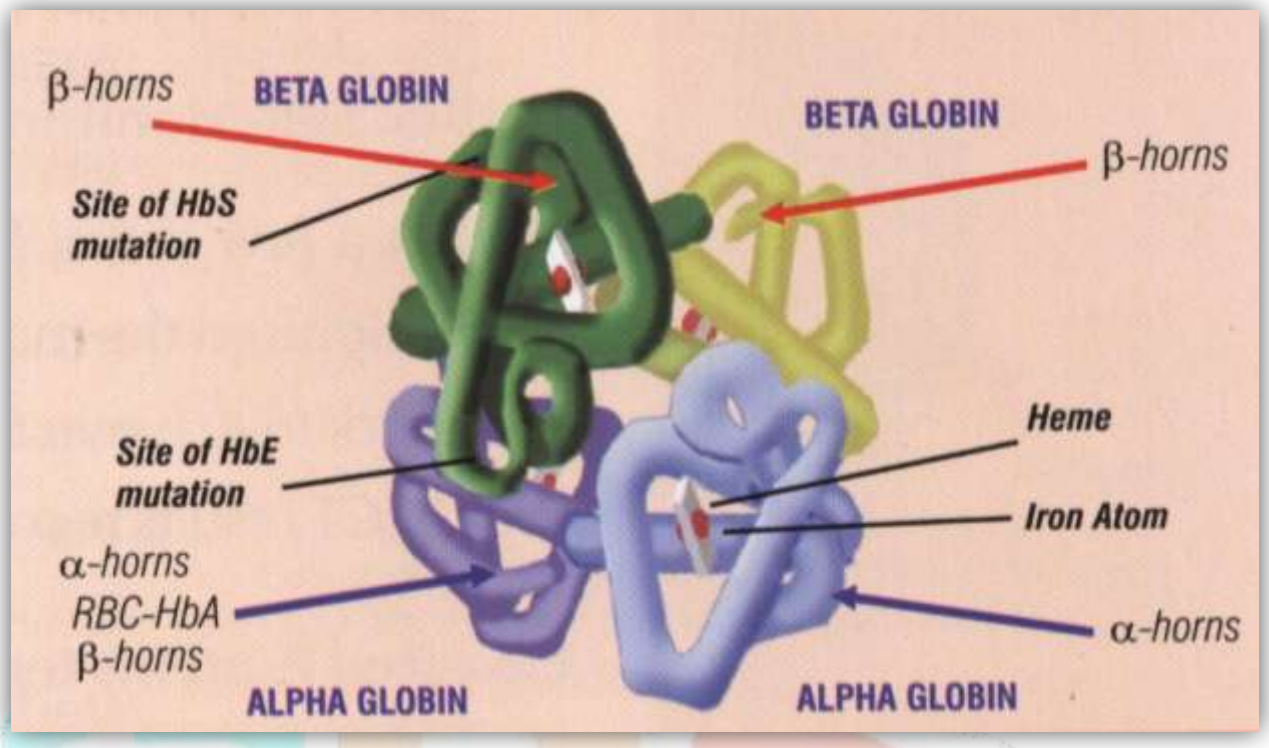

Figure 1 shows structure of hemoglobin

Iron and the porphyrin compound merge to produce metalloporphyrin, and it contains an approximate 0.34% of metal iron content. Fe indicates ferrous state of iron ion and helps heam to keep iron in ferrous state by globin. Keeping in view of normal adult hemoglobin, has HbA chains which is categorized into α and β chains and HbA2 –α and δ chain are present. A single chain is of a sequence of about 150 amino acids. The replacement of any one these amino acids by another, results in production of abnormal chain and abnormal Haemoglobin. For e.g. in Hb-S which is present in sickle cell anaemia. On the basis of amino acid sequence, the globin molecules are of several types. Globin chains are of α, β, δ, ε, etc .Haemoglobin level in humans is

- Normal Hb level in human is 14.5 gm/
- In Males 14-17 gm/% (gms per 100 ml)
- In Females 12-15 gm/%(gms per 100 ml)

The various types of Hemoglobin are

1. Hb F-Fetal hemoglobin
2. Hb A-Adult hemoglobin
3. Hb S-sickle cell disease
4. Hb C, Hb E-hemoglobinopathies

- Glycated Hb is formed by reaction between Glucose and Hb A.

The different types of Glycated Hb (GHb) are:

1. Fructose 1, 6 diphosphine –N-terminal Valine- Hba_{1a1}
2. Glucose 6 phosphate –N-terminal valine- Hba_{1a2}
3. Other CHO – N-terminal Valine- Hba_{1b}
4. Glucose –N-terminal valine- Hba_{1c}

- Hba_{1c} is normally less than 6% of Hb

1.3 Diabetes

Diabetes is also known as diabetes mellitus (DM), is disease having high blood sugar levels over a long period. The symptoms of diabetes are increased thirst, frequent urination and increased hunger. A diabetic patient suffers from many complications such as stroke, kidney failure, foot ulcers, heart disease and eye damage. As the pancreas not producing enough insulin to body results in diabetes.

The different kinds of diabetes mellitus are:

1. ***Type 1 diabetes mellitus***

As body fail to produce enough insulin in blood, person suffers from type 1 diabetes. It is also called as insulin-dependent diabetes mellitus (IDDM). Treatment of Type 1 diabetes is just giving insulin injections to patient.

2. ***Type 2 diabetes mellitus***

The cells fail to respond to insulin properly known as type 2 diabetes. As the development in disease insulin gets reduced. Type 2 DM is also known as non insulin-dependent diabetes mellitus (NIDDM). The effect of this disease is excessive body weight, not enough exercise and unbalanced food. Type 2 diabetic patients treated from medications with or without insulin which result in low blood sugar.

3. ***Gestational Diabetes***

Another kind of diabetes mellitus which frequently occur in pregnant women without checking blood glucose level results in high blood glucose. This diabetes is recovered after the birth of the baby.

The various Symptoms of Diabetes mellitus are found in untreated diabetic patient are loss in weight, frequent urination (polyuria), increased thirst (polydipsia), and increased hunger. The effect are developed quickly in weeks or months in type 1 diabetes, and the same effect usually develop slowly/absent in type 2 diabetes. The various other symptoms seen in diabetic patients are headache, itchy skin fatigue, slow healing of cuts, and blurry vision. As increase BG in the body results in glucose absorption in the lens of the eye, leads to change in shape of eye, resulting in blurred vision.

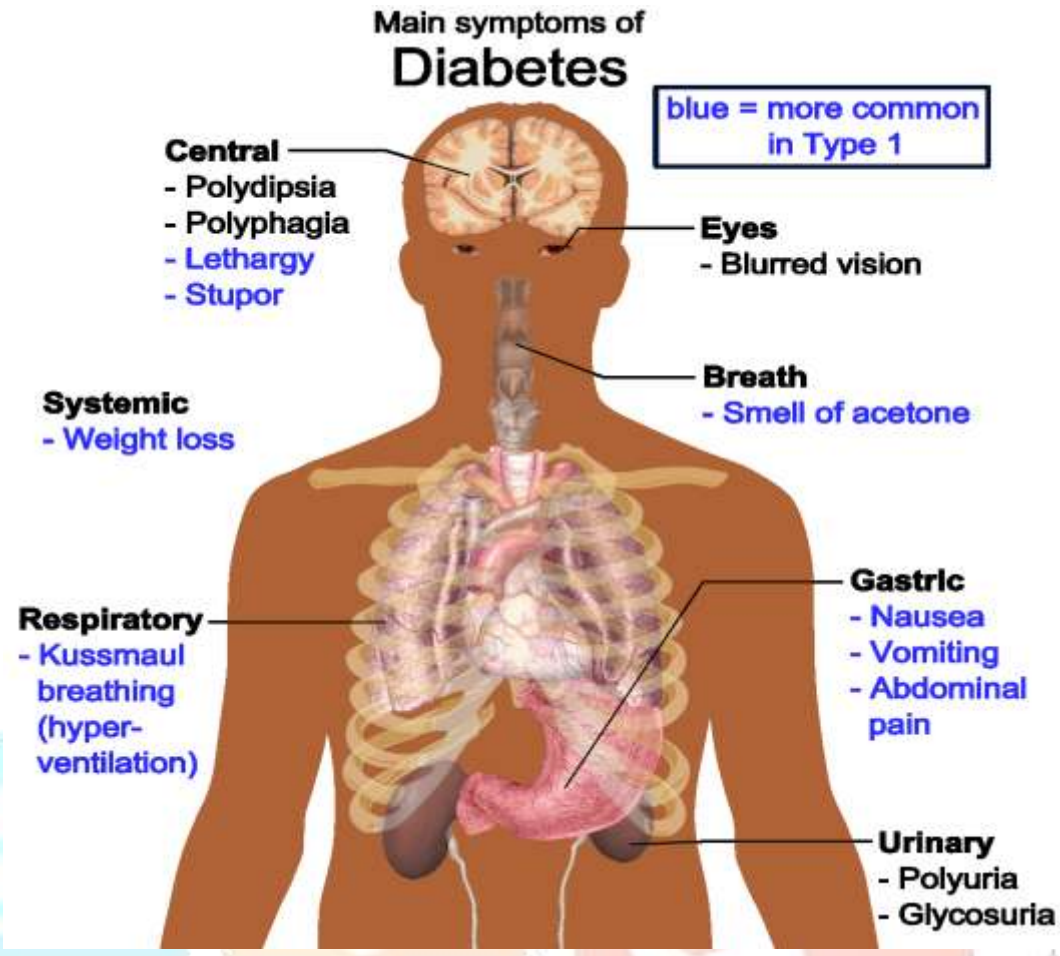

Figure 2 shows overview of symptoms of diabetes

1.4 Hyperglycemia

The meaning of hyperglycema in Greek is Hyper means excessive; -glyc means sweet and -emia means of the blood. As increase in amount of glucose circulates in the blood plasma cause hyperglycemia. In simple words hyperglycemia is high blood sugar in body [1].it generally occurs if the glucose level higher than 200 mg/bli.The symptoms will not start until higher glucose level such as approximate 250–300 mg/dl.The blood glucose (BG) level is measured in the following way:

- Millimole per litre (mmol/l) is the SI standard unit.
- United States, Japan, France, Egypt and Colombia measure glucose level as Milligrams per decilitre (mg/dl). mg/dl is obtained by multiplying mmol/L by 18.

Result of hyperglycemia

- Increased in mortality rate =16%
- Patient has long stay in hospital ,high cost hospitalization, changes in therapy often
- More patients found in intensive care unit.

Hyperglycemia hospitalized patient with diabetes mellitus (DM) is associated with growth rate in mortality (death) and morbidity (poor health condition). The aim of study is to obtain measurement of haemoglobin A1c and glucose insulin therapy is to implement to reduce readmission rate and cost individual

treatment.HbA1c is measure of diabetes care in large number of individuals identified as having a diagnosis of diabetes. The measurement of A1c at the time of admission of patient offers to assess the current therapy and to make changes in that therapy if indicated. We considered four groups of encounters:

(1) No HbA1c test performed.

(2) HbA1c performed and in normal range.

(3) HbA1c performed and the result is greater than 8% with no change in diabetic medications.

(4) HbA1c performed, result is greater than 8%, and diabetic medication was changed.

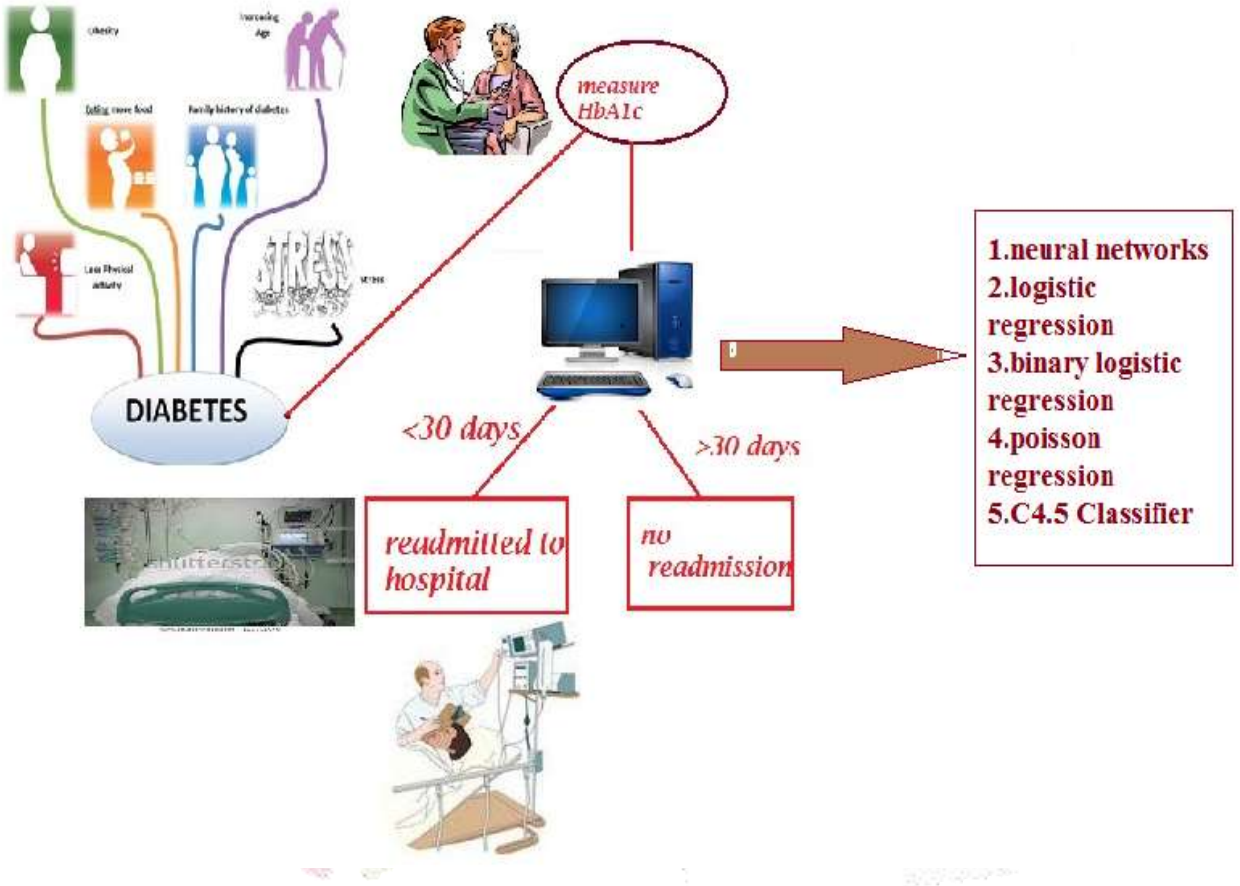

Figure 3 shows block diagram of diabetes

II. Data section

The dataset extracted from the database with 55 attributes. Dataset encounters information was extracted systematically from the database [2] includes encounter (a hospital admission of emergency, outpatient and inpatient),age(10-100),gender(male –female),race(causian,African american,asian,Hispanic),diagnosis is documented by various ICD-09 codes. Conducted laboratory tests of various patients and suggested medications during encounter. Measurement of A1c result to know if greater than 8 %(unhealthy) or <7%(healthy) which in turn decide the whether to readmit the patient or not within 30 days of hospitalization.

Table 1 shows description of dataset

Feature name	Description and values
Encounter ID	An unique identity of patient
Patient number	A unique identity of patient
Race	In includes Caucasian, Asian, African American, Hispanic
Gender	Male and Female
Age	The values lie intervals from 0-100
Admission type	Integer identity having values like emergency, urgent,elective,newborn etc
Discharge disposition	An integer identity that refers to discharged to home, expired etc
Admission source	The integer values refers to emergency room, physician referral, and transfer from hospital
Time in hospital	Integer number of days between admission and discharge
Number of lab Procedures	Number of lab tests performed during the encounter
Number of Procedures	Number of procedures (other than lab tests) performed during the encounter
Number of Medications	Number of distinct generic names administered during the encounter
Number of outpatient visits	Number of outpatient visits of the patient in the year preceding the encounter
Number of emergency visits	Number of emergency visits of the patient in the year preceding the encounter
Number of inpatient visits	Number of inpatient visits of the patient in the year preceding the encounter
Diagnosis 1	The primary diagnosis (coded as first three digits of ICD9); 848 distinct values
Diagnosis 2	Secondary diagnosis (coded as first three digits of ICD9); 923 distinct values
Diagnosis 3	Additional secondary diagnosis (coded as first three digits of ICD9); 954 distinct Values

Number of diagnoses	Number of diagnoses entered to the system
Glucose serum test result	Indicates the range of the result or if the test was not taken. Values: “>200,” “>300,” “normal,” and “none” if not measured
A1c test result	was greater than 8%, “>7” if the result was greater than 7% but less than 8%, “normal” if the result was less than 7%, and “none” if not measured.
Change of medications	Indicates if there was a change in diabetic medications (either dosage or generic name). Values: “change” and “no change”
Diabetes medications	Indicates if there was any diabetic medication prescribed. Values: “yes” and “no”
24 features for Medications	For the generic names: metformin, repaglinide, nateglinide, chlorpropamide, glimepiride, acetohexamide, glipizide, glyburide, tolbutamide, pioglitazone, rosiglitazone, acarbose, miglitol, troglitazone, tolazamide, examide, sitagliptin, insulin, glyburide-metformin, glipizide-metformin, glimepiride-pioglitazone, metformin-rosiglitazone, and metformin-pioglitazone, the feature indicates whether the drug was prescribed or there was a change in the dosage. Values: “up” if the dosage was increased during the encounter, “down” if the dosage was decreased, “steady” if the dosage did not change, and “no” if the drug was not prescribed
Readmitted	Days to inpatient readmission. Values: “<30” if the patient was readmitted in less than 30 days, “>30” if the patient was readmitted in more than 30 days, and “No” for no record of readmission.

III. Existing methods

3.1 Sliding scale insulin (SSI)

Insulin is the foundation of treatment for many people with diabetes. People with type 1 diabetes, and some with type2 diabetes, have to take several injections of insulin a day. This medication keeps their blood sugar in a normal range and prevents high blood sugar levels, which can help them avoid diabetes complications [3]. In SSI method, the dose is based on blood sugar level before meal. The higher blood sugar, the more insulin we take. SSI therapy has been around since the 1930s and first described by Elliton Joslin It’s most often used in hospitals and other healthcare facilities because it’s easy and convenient for the medical staff to administer.

3.1.1 Carbohydrate to Insulin Ratio

In SSI method, taking a certain amount of insulin for a certain amount of carbohydrate. For example, if your breakfast carbohydrate to insulin ratio is 10:1 and you eat 30 grams of carbohydrates, you would take 3 units before breakfast to cover your meal. This method also includes a "correction factor" which accounts for your premeal blood sugar.

3.1.2 How Sliding-Scale Insulin Therapy Works

In most sliding-scale insulin therapy regimens, your blood sugar is taken using a glucometer. This is done every six hours, or before meals and at bedtime — in total, about four times a day. The amount of mealtime insulin you get is based on your blood sugar measurements at those times. Usually fast-acting insulin is used

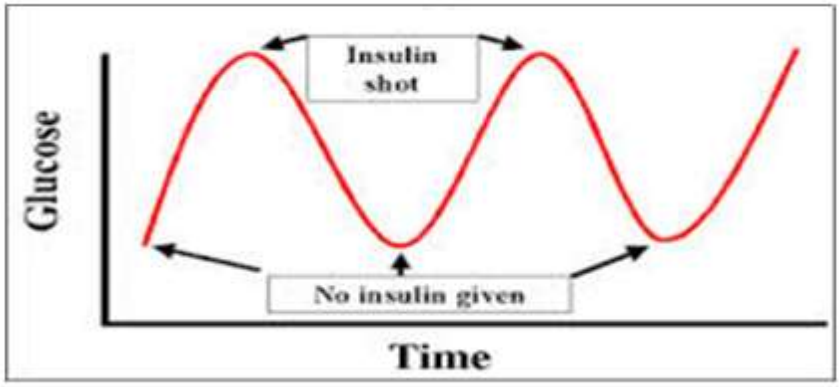

Figure 4 shows estimation of sliding scale insulin

3.2 70/30 insulin

A combination of 70% Insulin Isophane suspension and 30% insulin injection. As compared to regular insulin 70/30 insulin acts as intermediate insulin. The activity takes up to 24 hours duration of injection.70/30 is depending on medical dose, injection, temperature, blood supply, and physical activity.70/30 is referred as sterile suspension. The concentration present in 70/30 is 100 units/ml.

Figure 5 shows 70/30 insulin

3.3 Basal and bolus insulin therapy

Basal and bolus insulin is type of insulin which involves consumption of many numbers of injections in the day. After each meal basal and bolus insulin injection is taken to compare how non diabetic person generate insulin. 70/30 Insulin is given to both type 1 and type 2 diabetes.

Figure 6 shows basal bolus insulin

BBI is long acting insulin to keep BG level constant at the time of fasting and also it is short acting insulin to avoid increase in blood glucose level by providing separate injection during meals [4]. Basal insulin known as back ground insulin to keep BG level at consistent level. Bolus insulin provided during meals period to control the blood glucose level .Bolus insulin reacts quickly in patient. The advantages of BBI are

- BBI compares how body quickly release insulin in body.
- Flexible

The disadvantages of BBI are

- It involves more insulin injections each day
- It should be comfortable with injecting at meal times

IV. Proposed Method

4.1 Neural networks

Neural network is also known as artificial neural network (ANN). Dr. Robert Hecht-Nielsen invented the first neurocomputers and defines the neural network as ,"neural network is a computing system which consists of number of interconnected, simple nodes, and each node process the data by their dynamic state response to output.

4.1.1 Neural network model

Neural networks model shown below in figure 7 consists of 3 layers such as input layer, hidden layer, and output layer. These layers consists simple, interconnected number of nodes. In neural network the patterns are given as input to network through the input layer, and these input layers make number of connections with hidden layers where actual process of pattern is undergone through a system of weighted connections. After processing the patterns the hidden layer link the result to output layer as shown in figure 7.

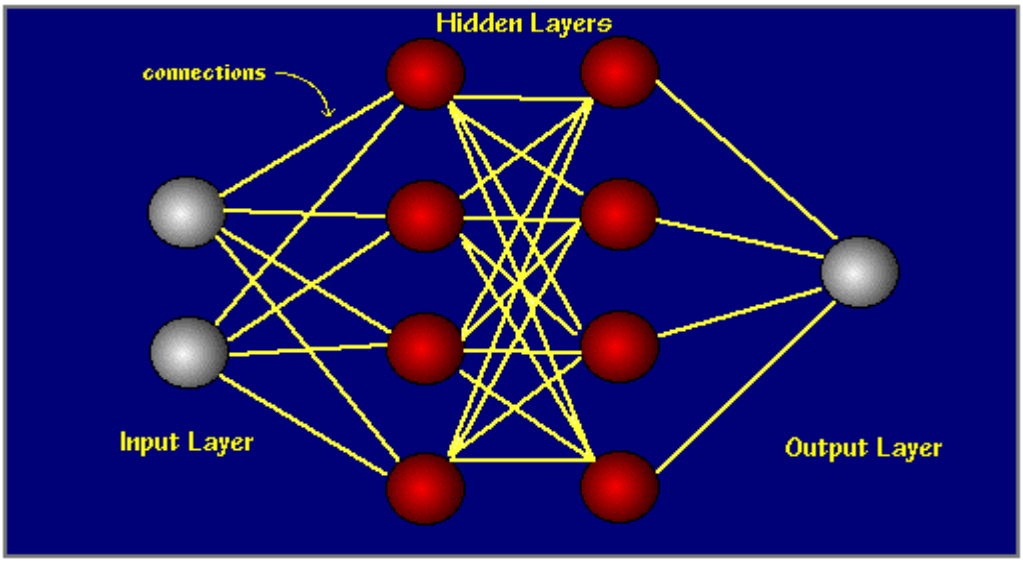

Figure 7 shows neural network model

Neural networks is demonstrated using one of rule known as backpropagation neural networks (BPNNs)[6].Backpropagation stands for the backwards propagation of error. In simply saying neural network process pattern and present initially pattern with some random guess of output as expected output. Neural networks compares how far the present output differ from actual output expected and use backpropagation method to change in connections of weights so as to reach the actual output as shown in figure 8.

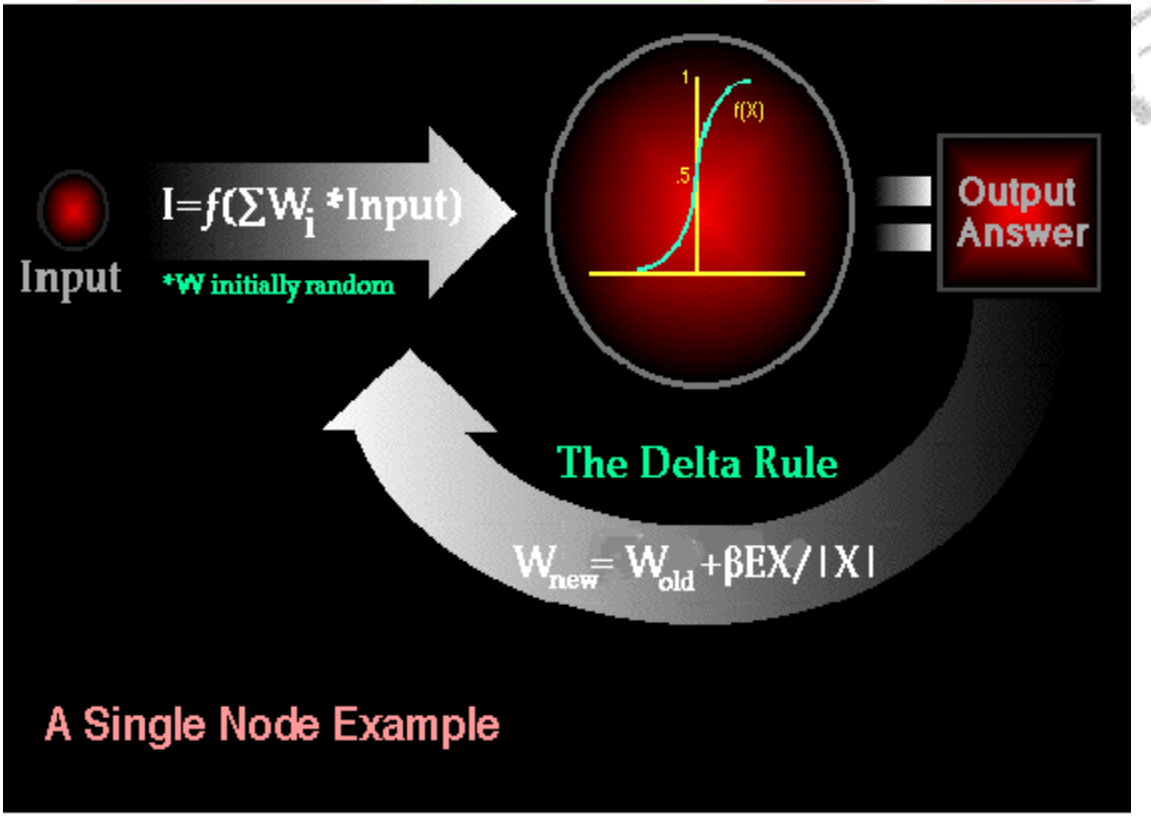

Figure 8 shows example of network model

4.2 Poisson regression

The regression analysis that is method involves to count data and tables is Poisson regression. Considering dependent variable Y and apply logarithm of an expected value of Y value can be used by linear combination of using independent parameters. Poisson regression model is also called as log linear model because as it is used to model contingency tables. Poisson regression models is function that assuming probability distribution of response and use link function as generalized linear models with the logarithm.

Poisson regression use rate data in which rate is defined as count of events occurring for particular unit of readings and divided by some readings of particular unit called exposure. Consider the example biologists collect number of species of trees and calculate rate as the number of tree species found in per square kilometre. In general rate of event (exposure) is calculated as event/unit time, by which observation window changes for each unit. In above example unit area is exposure. When the exposure variable enters to right hand side and parameters estimation is considered to 1, this is handled as offset in Poisson regression.

$$\log\left(\mathrm{E}(Y \mid x)\right) = \log\left(\text{exposure}\right) + \theta' x$$

$$\log\left(\mathrm{E}(Y \mid x)\right) - \log\left(\text{exposure}\right) = \log\left(\frac{\mathrm{E}(Y \mid x)}{\text{exposure}}\right) = \theta' x$$

While calculating parameters for regression we consider the value θ that is used maximize the expression in the form

$$\sum_{i=1}^{m} \log(p(y_i; e^{\theta' x})),$$

m is number of samples in the data set and it is the probability mass function in the Poisson distribution. If we apply optimization method instead of maximize

$$\sum_{i=1}^{m} \log(p(y_i; e^{\theta' x})) - \lambda \|\theta\|_2^2,$$

4.3 Logistic Regression

Logistic regression is a type of regression used for classification model as well as prediction model. It is using binary variable (x) and used to predict the result of dependent variable(y).It is used to estimate parameters of qualitative response model. If the dependent variable is binary (i.e. only two variables) is called binary logistic regression. If the dependent variables is more than two variables is called multinomial logistic regression. It finds relation between the dependent variable and independent variables.

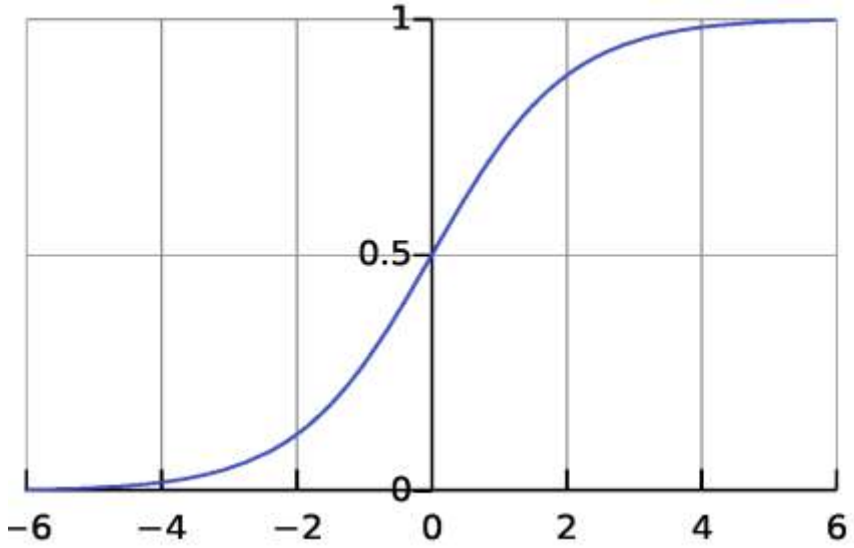

Figure 9 logistic function

Logistic function used in logistic regression takes values which lie between 0 and 1.

$$F(t) = \frac{e^t}{e^t + 1} = \frac{1}{1 + e^{-t}},$$

t is a linear combination of variables. Logistic function is written as:

$$F(x) = \frac{1}{1 + e^{-(\beta_0 + \beta_1 x)}}.$$

Logistic function estimate result as probability of dependent variable either success or failure.

4.4 C4.5 classifier

C4.5 is method first developed by Ross Quinlan which is used to construct the decision tree. C4.5 is an extension of ID3 method/algorithm developed by Quinlan.it is used for classification and is referred as a statistical classifier.C4.5 chooses the attribute of the dataset for each node of the tree, splits set of dataset into subsets into one another class. The splitting is based on difference in entropy. The attribute present in one node having highest information gain is chose to make the decision.C4.5 algorithm depends on the smaller sub nodes.

The condition of C4.5 algorithm is

- The data in the nodes should be same class and it creates the leaf node for the decision tree to choose the class.
- C4.5 generates a decision tree where each node is high using the expected value that belongs to each class.
- C4.5 creates a node higher the tree using the expected value of unseen class encountered.

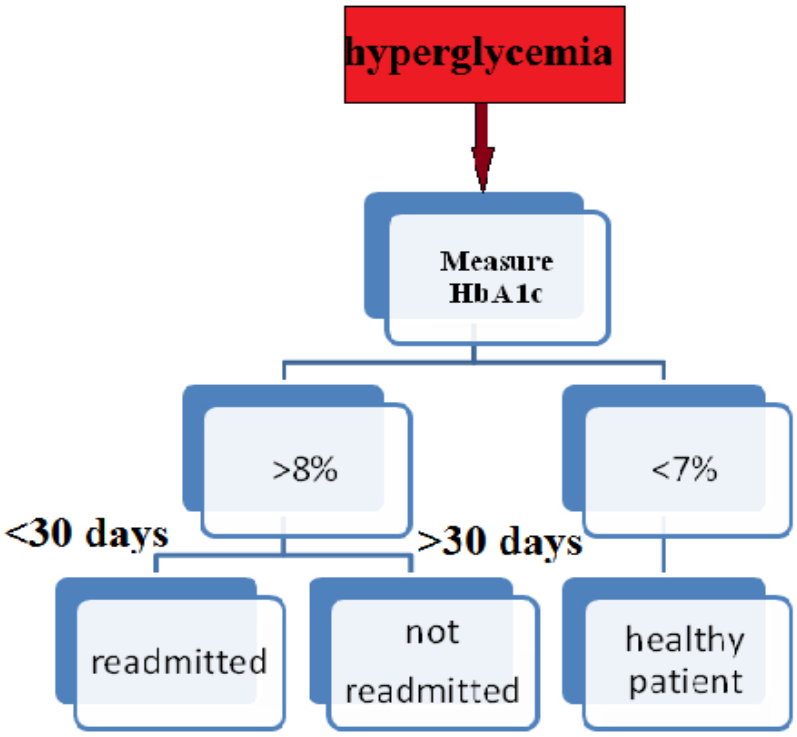

Figure 10 shows graphical representation of diabetes

4.5 Binary logistic regression

Binary regression is also called as binomial regression is a method use to predict the only two outcome variables such as success or failure from the independent variables.One independent variable, one dependent variable is given as

$$P(Y) = \frac{1}{1 + e^{-(b_0 + b_1 x_1)}}$$

P: probability of Y occurring

e: natural logarithm base (= 2,7182818284…)

b0: interception at y-axis

b1: line gradient

X1 predicts the probability of Y.

The overall performance is to compute p-value.

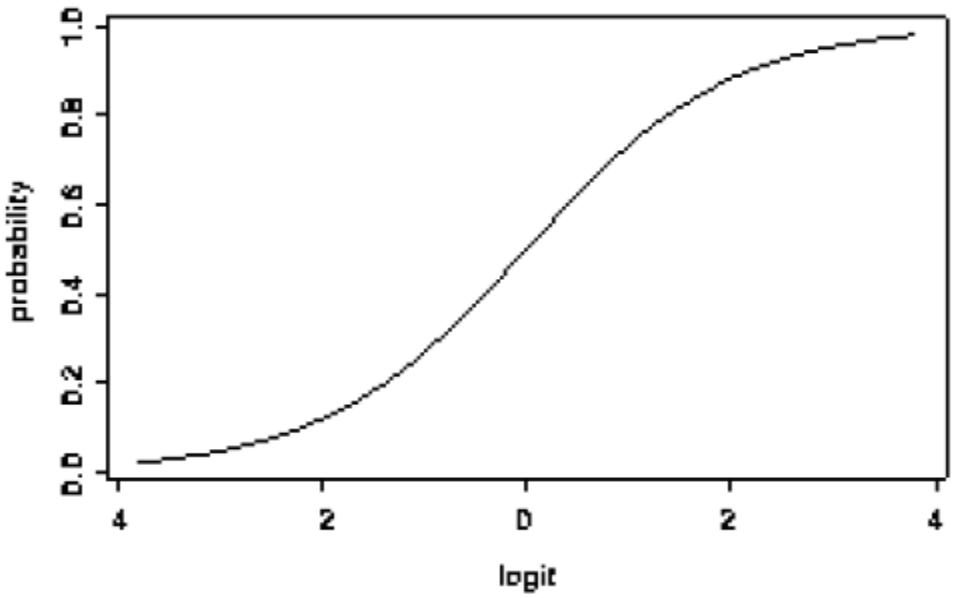

Figure 11 shows binary function

V. Result

Diabetic patient having insulin therapy has poor survival, poor clinical outcomes, nurse has less knowledge of treatment to hyperglycemic patient. Type 1 and type 2 diabetic patient's clinical data is extracted and applying to different methods to shows decrease in mortality in hyperglycemic Patients even decrease in readmission rate to hospital. Decrease in intensive care unit (ICU) entrance of critically ill patients. Patient with lowest and highest A1c result has mortality rate of 4.6% and 2.8% from regression method. The diagnosis may suggest the relationship between measurement of HbA1c and readmission rate of diabetic patient.

VI. Discussion

The result from the present analysis represent a preliminary observation with limitations to such large health records .in addition to the limitations of working with large clinical datasets discussed earlier, the study is limited in just providing various insulin to diabetic patient. Data with some alterations like removing noisy data appear to suggest insulin therapy based on HbA1c measurement and readmission to hospital may be warranted.

VII. Conclusion

The decision is to obtain HbA1c measurement of diabetes to improve patient outcomes and cost for care of individual treatment. The aim is to have greater attention to diabetes mortality rate, mitigating poor surgical outcomes, early detection and initiation of therapy of hyperglycemic hospitalized patients.SSI,70/30 insulin,BBI, neural network, logistic regression, binary logistic regression,poisson regression,C4.5 classifier methods are suggested to reduce readmission rate, mortality.

References

[1] G. E. Umpierrez, S. D. Isaacs, N. Bazargan, X. You, L.M.Thaler, and A. E. Kitabchi, "Hyperglycemia: an independent marker of in hospital mortality in patients with undiagnosed diabetes," Journal of Clinical Endocrinology and Metabolism, vol. 87, no. 3, pp. 978–982, 2002.

[2] A. Frank and A. Asuncion, UCI Machine Learning Repository, University of California, School of Information and Computer Science, 2010.

[3] D. Baldwin, G.Villanueva, R.McNutt, and S. Bhatnagar, "Eliminating inpatient sliding-scale insulin: a re-education project with medical house staff," *Diabetes Care*, vol. 28, no. 5, pp. 1008–1011, 2005.

[4] M. C. Lansang and G. E. Umpierrez, "Management of inpatient hyperglycemia in noncritically ill patients," Diabetes Spectrum, vol. 21, no. 4, pp. 248–255, 2008.

[5] R. Vinik and J. Clements, "Management of the hyperglycemic inpatient: tips, tools, and protocols for the clinician," Hospital Practice, vol. 39, no. 2, pp. 40–46, 2011.

[6] R. M. Bergenstal, J. L. Fahrbach, S. R. Iorga, Y. Fan, and S. A. Foster, "Preadmission glycemic control and changes to diabetes mellitus treatment regimen after hospitalization," *Endocrine Practice*, vol. 18, no. 3, pp. 371–375, 2012.