A Study of Using Fuzzy Logic based System for Adaptation of Precise Insulin Dosage for Type II Diabetes Patients

A project submitted

by

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to

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Dedicated to my parents, sisters and supervisor

Certification Statement:

This is to certify that the project titled “A study of using fuzzy logic based system for adaptation of precise insulin dosage for type II diabetes patients” submitted for the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy from the Department of Pharmacy, BRAC University resembles my own work under the supervision of Md. Rubayat Islam Khan, Senior Lecturer, Department of Pharmacy, BRAC University and that appropriate credit is given where I have used the language, ideas or writings of another author.

Signed,

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Date:

Countersigned by the Supervisor,

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Date:

Acknowledgement:

Foremost, all the praises to Allah, Who is the source of our wisdom and, He Who has guided me in my studies, my academic career, and this very project.

I would like to start by thanking Rubayat Islam Khan, Senior Lecturer, Department of Pharmacy, BRAC University, without whom, execution and completion of my thesis would never be possible. My heartiest gratitude to him for his consistent supervision, which has helped me to execute the thoughts into work. My commitment to conduct a survey would have been amiss without his efforts, instructions, intelligence and assistance.

I am also beholden to Professor Dr. Eva Rahman Kabir (Chairperson, Department of Pharmacy, BRAC University), who always encourages any endeavor to computational expertise. I thank her for facilitating computer lab amenities.

Moreover, I would like to show a token of respect to my parents, who have always encouraged me with my work and has been supportive throughout this research. My sisters have shown an immense enthusiasm in my work and encouraged me with their youthful mindset to find excitement in my work.

Lastly, I am greatly indebted to the people who took part in this survey and shared their information. Without their participation, my work would have not been complete. I am also thankful to my friends for their support.

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List of acronyms:

PPG: Postprandial glucose

CI: Computational Intelligence

MATLAB: Matrix Laboratory

FL: Fuzzy Logic

ANN: Artificial Neural Network

GDM: Gestational Diabetes

Abstract:

The prime purpose of this study is to design a precise daily insulin dosage for type II diabetes patients, who are on insulin regimen currently. This more precise and accurate dose is designed with the help of fuzzy based system. The dose is adjusted by keeping several factors such as postprandial glucose level and duration of taking insulin are being considered. To conduct this study 10 type II diabetes patients, undergoing insulin treatment, were randomly selected and the information was collected. The data were utilized to develop rules for a fuzzy based system in MATLAB. This system assists to generate an output that is required to compare with the prescribed doses of insulin by the physicians. This method calculates the total daily insulin dose depending on each individual factor and the generated output are more likely to provide better control over patient's blood glucose level.

Chapter I

1. Introduction:

According to a study conducted by WHO in 2015, diabetes is responsible for the death of 1.6 million people in 2015, up from less than 1 million in 2000. It is the 6th cause of top 10 common causes of death throughout the world. (“The top 10 causes of death,” n.d.)

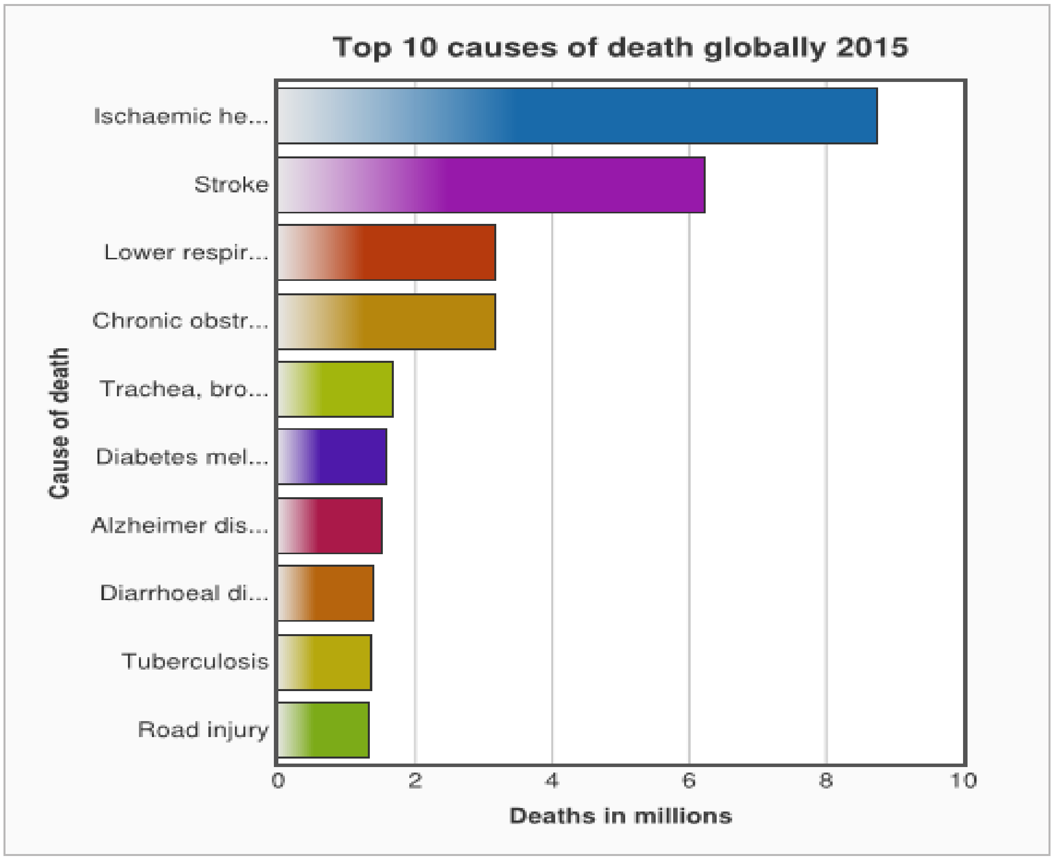

Figure 1.1: Graph that Represents the Top 10 Causes of Death Globally (“The top 10 causes of death,” n.d.)

In human body, one of the most important hormones is insulin and the secretion and production of this hormone is regulated in a controlled manner by the body. If there is any abnormality in these procedures, the metabolic homeostatis is impaired and this results in metabolic disorders or diseases such as diabetes.(Tian, Xu, Du, & Fu, 2018) The secretion of insulin is higher at daytime; whereas, it is lower during nighttime. (Leung, Huggins, & Bonham, 2017) A traditional way of thinking includes that insulin secretion is mostly related to carbohydrate intake, though the amount of fat and protein intake can also influence this. (van der Hoogt, van Dyk, Dolman, & Pieters, 2017)

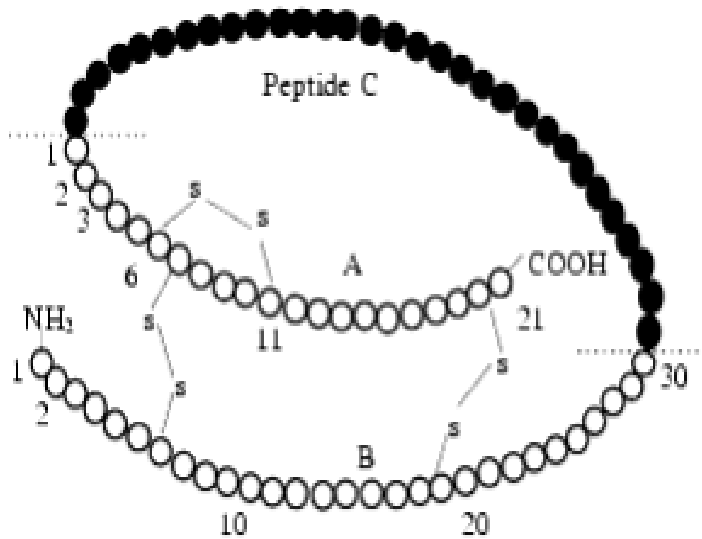

Figure 1.2: Chemical Structure of Insulin ("Insulin, chemical structure and metabolism - Pharmacorama," n.d.)

Diabetes is not a single disease. Rather, it can be designated as a divergent group syndrome described by inflated blood glucose attributed to a relative or absolute deficiency of insulin. This includes the following types- 1) Type I or Insulin-dependent diabetes mellitus, 2) Type II or Non-insulin-dependent diabetes mellitus, 3) Gestational diabetes, and 4) Diabetes due to other causes such as genetic defects or medication. ("Lippincott Illustrated Reviews," n.d.)

1.1. Type I or Insulin-Dependent Diabetes Mellitus:

Type I diabetes was previously known as insulin-dependent, juvenile or childhood-onset diabetes. ("Lippincott Illustrated Reviews," n.d.) It appears when the body is unable to produce sufficient amount of insulin that is desired. Type I diabetic patient requires everyday supple of insulin to control the blood glucose level. This type of diabetes is not preventable as the body is unable the required amount of insulin to conquer the sugar concentration in blood. This type of patient cannot survive, if insulin is not provided from outside source. Excessive urination, thirst, overeating, weight shaving, difficulty with vision and fatigue are some of the common symptoms of this type of diabetes. Whereas, a less common risk of type I diabetes includes periodontitis. (Duda-Sobczak, Zozulinska-Ziolkiewicz, & Wyganowska-Swiatkowska, 2018) The definite reasons behind type I diabetes are unknown. A common conception of the reason behind this disease is that it is product of convoluted synergy between human genes and other environmental aspects though no such evidence of such risk factors in major number of incidence. (Roglic & World Health Organization, 2016) It prevails mainly in children and adolescents.

1.2. Type II Diabetes or Non-Insulin-Dependent Diabetes:

It was previously known as non-insulin-dependent or adult-onset diabetes, onset when the body is incompetent to yield the necessary amount of insulin for a human body to possess the blood sugar assembly. It is responsible for the vast majority of people with diabetes around the world. ("Worldwide trends in diabetes since 1980," 2016) The symptoms are similar with type I diabetes to some extent, though these are prominently prevailing. However, as the symptoms remain hidden, in case of most of the patients the disease is diagnosed delayed. In some cases, this even remains undiagnosed for several years. Previously, it was observed only in adults, but nowadays children are also seen suffering from type II diabetes. Reciprocity of different factors, genetic and metabolic, plays crucial role in type II diabetes. Ethnicity, previous family history combines with age, obesity, non-nutritional food habit, lace of exercise and consuming tobacco boost the risk of type II diabetes in personnel. (Roglic & World Health Organization, 2016)

1.3. Gestational Diabetes (GDM):

Pregnant women are the sufferer of this. In this type of diabetes, blood glucose level aggravates but remains above the diabetes range. (Ahmad et al., n.d.) This type of diabetes also carries a long-term risk of type II diabetes. (Finucane, Paciorek, Danaei, & Ezzati, 2014) Gestational diabetes sometimes induce complications during pregnancy and as well as in the infants. It is diagnosed through prenatal screening. (Roglic & World Health Organization, 2016) Age plays a very crucial role in gestational diabetes. Higher the reproductive age of woman, higher the risk of GDM. Despite of overweight issues, weight gain in pregnancy, history of diabetes in family, history of gestational diabetes during the previous pregnancy or intrauterine death, bringing forth with congenital abnormality, and glucosuria during pregnancy are also some of the major causes of this type of diabetes. These phenomena contribute largely as the root cause of GDM.

1.4. Complications of different types of diabetes:

If diabetes is not well disciplined, it bears the authority to endanger lives. Diabetes ketoacidosis (DKA) in type I and II diabetes is a condition that is a result of abnormally elevated blood glucose level. This condition can have life threatening impact. Hyperglycemia has an association with periodontal diseases such as periodontal tissues. (Novotna, Podzimek, Broukal, Lencova, & Duskova, 2015) Abnormally low blood glucose level is also responsible for various life-appalling conditions like seizures or syncope. Obesity-related type II diabetes is now spreading its veraciousness among youth and adults under the age of 45. (Gregg, Sattar, & Ali, 2016)

1.5. Glycemic control and diabetes mellitus:

The amount of people suffering from diabetes may rise from 415 million in 2015 to 642 million in 2040 worldwide among which 80% live in under-developed or developing countries. ("IDF Diabetes Atlas," n.d.) WHO has also declared that diabetes had reached epidemic proportions, which is predicted to be observed in developing countries. (World Health Organization & International Diabetes Federation, 2006) The prevalence of diabetes is predicted to increase developing countries. It may rise upto 5.6% from 4.2% and in Bangladesh 3.9% to 4.8% during the period of 2000-2030. ("2. Classification and Diagnosis of Diabetes," 2016) There are several factors that affect diabetes mellitus and one of them is blood sugar level. When a person is suffering from diabetes, he or she might face high or low blood sugar level from intermittently. When the blood sugar level is below the normal range, which is 80–130 mg/dl or 4.4–7.2 mmol/L, it is called hypoglycemia whereas hyperglycemia occurs when the blood glucose level is above this range. Glycemic control holds a compelling role in governing of diabetes. Fasting plasma glucose (FPG), HbA1c, pre-meal glucose level, post-meal glucose level is monitored to manage diabetes. The ideal ranges of diabetes are based on the outcomes of clinical trials under strict monitoring. Multiple evidences are present that indicate that hyperglycemia or increased blood glucose level has a major role in aggravating the condition of diabetes. Intensive diabetes control could reduce the development of microvascular complications in type 2 diabetes. (Klein, 1995)&(Turner et al., 1998) The first and foremost concern of treating a diabetes patient is to attain control over blood glycemic level. The American Diabetes Association recommended target of good glycemic control is expressed as HbA1C < 7%. (Klein, Klein, Moss, Davis, &

DeMets, 1984) The post meal blood glucose level, which is also named as postprandial glucose (PPG), contributes to suboptimal glycemic control. Postprandial means post meal or after a meal. Therefore, PPG or postprandial glucose concentrations hint to plasma glucose concentrations after taking meal. Postprandial hyperglycemia is also one of the root reasons of glucose imbalance, which is linked to type II diabetes. It is significantly amplified in diabetic patients who have hyperglycemia when fasting. There are multiple factors that are important in determining the PPG profile. The fasting (usually 8-10 hours) plasma glucose concentration, in people who does not have diabetes, is 70-110 mg/dl, which usually increases after 10 minutes of starting of a meal. This incidence takes place due to absorption of carbohydrate the food taken. The amount of carbohydrate absorbed from the food, secretion of hormones such as insulin and glucagon play a critical role in the determination of PPG profile. In harmony, they can affect the metabolism of glucose in the liver and peripheral tissues. The ultimate consequence and the time to reach the peak plasma glucose concentration rely on diverse aspects for instance, time of food intake, the amount of food, and the type of meal they take. If a person is not suffering from diabetes mellitus, his plasma glucose concentration peak is within 140 mg/dl, nearly 60 minutes after taking meal. The concentration, after 2-3 hours, returns back to preprandial glucose levels but the carbohydrate absorption continues up to 5-6 hours' status post the meal. In case of type I diabetic patients, the time to reach the highest insulin concentration is dependent on the route of administration, type and quantity of insulin; whereas, the time to reach to reach the highest insulin concentration is delayed in type II diabetic patient. ("Postprandial Blood Glucose | Diabetes Care," n.d.)

Determination of PPG profile is vastly depended on various elements. In people suffering from type I and type II diabetes mellitus, the aspects that can contribute to reach exalted level of blood sugar secretion are any deviation from normal range of insulin and glucagon secretion, uptake of hepatic glucose, decreased production of hepatic glucose, and glucose uptake in peripheral tissues. As it usually takes 5-6 hours for the absorption of food in both diabetic and non-diabetic patient, the optimal time to measure PPG or postprandial glucose concentration needs to be determined. A measurement of plasma glucose 2 h after the start of a meal is practical, generally approximates the peak value in patient with diabetes, and provides a reasonable assessment of postprandial hyperglycemia in general. Specific clinical conditions, such as gestational diabetes or pregnancy complicated by diabetes, may benefit from testing at 1 h after the meal.

("Postprandial Blood Glucose | Diabetes Care," n.d.) For better glycemic control, insulin therapy is usually recommended or prescribed by the physicians depending on age, gender, BMI or other diseases of the patient. There for this has to be more precise for individuals suffering from diabetes. (Jayaraj, Cherian, & Vaidyanathan, 2009) & (Mirouze, 1983) This study is conducted to correlate the postprandial glucose level and type II diabetes mellitus and the role of hyperglycemia in type II diabetes patients. By observing the influences and analyzing the numerical values and with the help of computational technology designing a precise dose of insulin is the ultimate target of this research.CI (Computational intelligence) techniques for example, FL (Fuzzy Logic) and ANN (Artificial Neural Network) have been being used in different experimental analysis or research based works.

1.6. Fuzzy logic:

In this era, a new addition of our lives is computational intelligence. It has been used to serve humankind for its betterment. CI is basically dominating the health care system currently with its aptitude. It is dealing many complicated problems or disputes by developing intelligence systems. As per the traditional concept, FL involves encoding of human intelligence in preliminary resultant structure. (Cheung et al., 2001) It basically deals with logical reasoning of vague statement. (Le & Tran, 2018) The antecedent's provision of each rule is being matched after coming across the brand-new data's. Consequent clauses are entrenched if the antecedents match with the previous data. The action keeps going on until it derives to a satisfying or explainable result. If not, then no other rule, new or previous, can be fired. The fuzzy logic has been verified to be very convenient in the medicine sector in the past decade. (Cheung et al., 2001)Therefore, it is basically a way of interpreting human logic. The process of taking decisions by human, which usually involves all the probable solution between values of "Yes or "No", are being imitated by FL. The regular procedure of a computer involves reading out a specific input and then turns it into a definitive output "True" or "False", which in human language can be interpreted as "Yes or "No". (tutorialspoint.com, n.d.)

The inventor of fuzzy logic, Lotfi Zadeh, observed that unlike computers, the human decision making includes a range of possibilities between YES and NO, such as – certainly yes, possibly yes, cannot say, possibly no and certainly no.Precisely, fuzzy logic endeavors with the probability of input in order to attain output. (tutorialspoint.com, n.d.)

1.6.1. Implementation of fuzzy logic:

Fuzzy logic can easily be implemented in different ways such as in different types of systems for instance micro-controllers to large networked professional system or on hardware or software.

1.6.2. Necessity of fuzzy logic:

It is helpful in use for commercial purposes and practical purposes as it can hold authority over machines and consumer products. Fuzzy logic gives logical interpretation and helps to justify uncertainty in engineering.

1.6.3. Fuzzy Logic Systems Architecture:

The FL system architecture is composed of four main parts. First one is Fuzzification Module that works by altering crisp numbers, which were used as inputs into fuzzy values. The fuzzification module is able to alter the input signal and breach it into five parts, which are LP (Large positive), MP (Medium positive), S (Small), MN (Medium negative) and LN (Large negative). Second part is Knowledge Based that works as an inventory controller, when to store IF-THEN rules provided by the experts. The next part is Inference Engine that replicates the human reasoning process through creating fuzzy inference on the IF-THEN rules and the inputs. The final part is Defuzzification Module in which fuzzy values are obtained by transforming it with the help of engine inferring into a crisp value. (tutorialspoint.com, n.d.)

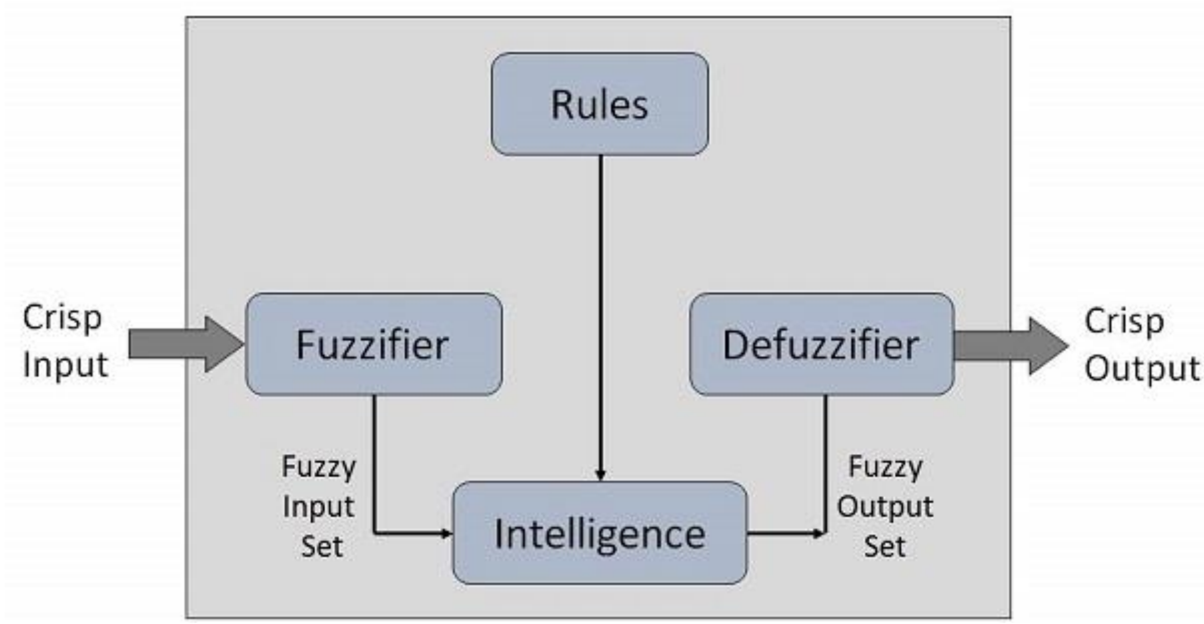

Figure 1.3: System Architecture of Fuzzy Logic (tutorialspoint.com, n.d.)

1.6.4. Membership Function:

The fuzzy variables are monitored and controlled by the the membership function.

Analysis of lingual conditions and graphical representation of fuzzy variables are performed by membership function. The definition of a membership function for a fuzzy set A on the universe of discourse X can be displayed as $\mu_A:X \rightarrow [0,1]$. In this definition, every feature of X is arranged in such a way that it will give a value amid 0 and 1, which is called membership value or degree of membership. The degree of membership of the element in X to the fuzzy set A is assessed by the degree of membership. The x axis of this graph represents the universe of discourse and the y axis is for degrees of membership in the [0, 1] interval. A numerical valued can be fuzzified by different membership function. Use of simple or complex membership function does not change the precision of the output. Below, the membership functions for LP, MP, S, MN, and LN are represented with the help of a graph. Here, as an example, a graph has been displayed that demonstrates the input of voltage and its membership function. It indicates that the 5-level fuzzifier varies from -10 volts to +10 volts. Alterations in the corresponding output are also observed. There are several available shapes of membership function, which includes trapezoidal, singleton or Gaussian, but the most widely used and most popular shape is the triangular membership function shape. (tutorialspoint.com, n.d.) One of the major drawbacks of FL membership is the requirement if high speed. (Moniem & Saleh, 2012)

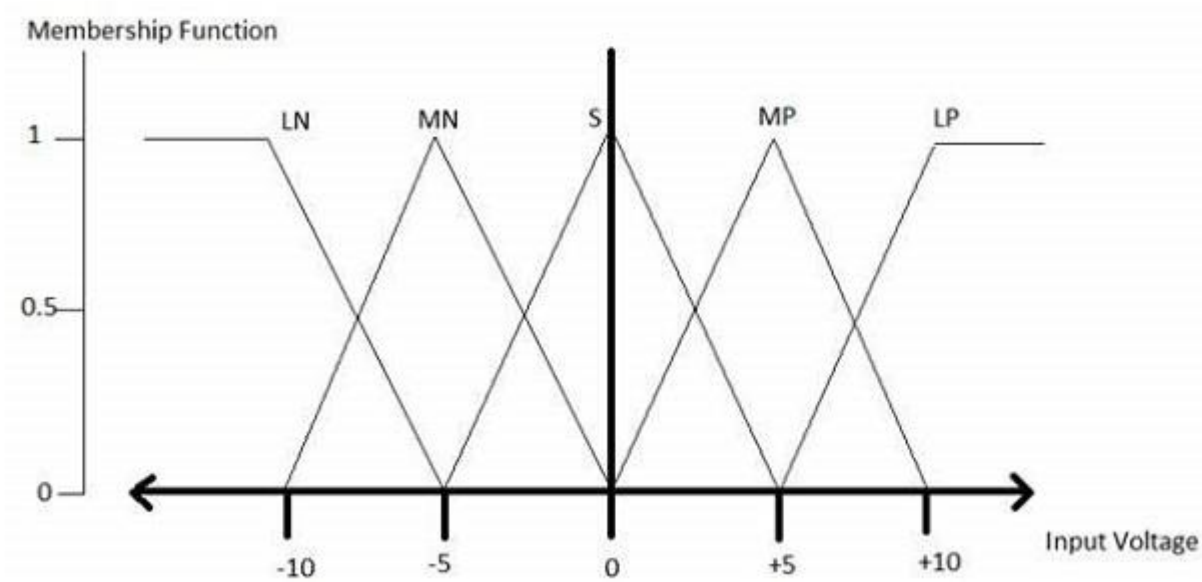

Figure 1.4: Membership function's example. (tutorialspoint.com, n.d.)

1.7. MATLAB:

MATLAB is a software that is extensively used for research purposes. It also aids on teaching applications on control and automation. This software has a powerful linear algebra tool with toolboxes, which helps to function MATLAB its basic claims with a synergistic open environment. (Besta, Kastala, Ginuga, & Vadeghar, 2013) It works by using simple expressions in command window. (Attaway, 2019)

Chapter II

2. Materials and Methods

Several methods and equipment were used to conduct this research to accomplish the study completely and to reach the ultimate goal.

2.1. Patient population:

10 type II diabetes patients receiving insulin treatment were inconsistently selected from Dhaka, Bangladesh including 7 males and 3 females. The information collected from each individual are postprandial glucose level, the duration of receiving insulin treatment, and the amount of insulin prescribed by the physician. Each patient was informed about the method and goal of this survey and the information was collected with their consent and they were cognizant of all the facts.

2.2. Calculation method and computational tools for insulin dosage:

Developing the method and data analysis was done with the assistance of MATLAB; whereas, a fuzzy based interface developed in MATLAB assisted in designing the dosage of insulin. The input variables include the factors that were collected during the data collection and the output is the obtained insulin dose. The basic approaches include- quantification of insulin dosage on the basis of average postprandial glucose level and quantification of insulin dosage on the basis of the duration of receiving insulin treatment. To amalgamate these methods of insulin dosage and receive the fuzzy based output, patient details were used to calculate insulin dosage separately using each method. The calculations are manifested in table 2.1 and 2.2. Table 2.1 resembles calculated insulin dosage considering the average postprandial glucose level of the patients. On the other hand, table 2.2 shows the insulin dosage considering the duration of receiving insulin treatment.

Table 2.1: Prescribed Insulin Dosage Considering the Average Postprandial Glucose Level of the Patients

Pt. No.	**Average post prandial glucose level**	**Calculated insulin dose**
1.	6.5	14
2.	8.0	12
3.	8.0	10
4.	10.0	40
5.	9.0	34
6.	7.0	18
7.	10.0	40
8.	7.0	17
9.	11.5	50
10.	7.0	14

Whereas, table 2 shows the calculated insulin dosage depending on the duration, for which the patient is receiving insulin treatment.

Table 2.2: Prescribed Insulin Dosage Depending on the Duration of Receiving Insulin Treatment

Pt. No.	**Average post prandial glucose level**	**Calculated insulin Dose**
1.	1.0	14
2.	7.0	12
3.	7.0	10
4.	9.8	40
5.	18.0	34
6.	2.0	18
7.	20.0	40
8.	6.0	17
9.	27.0	50
10.	11.0	14

Chapter III

3. Methodology:

3.1. Objective:

The prime goal of this research was to design a precise insulin dose for type II diabetes patients to help them control their blood glucose level.

3.2. Research design and methods:

The study was inaugurated with developing a questionnaire. Before the generation of questionnaire, papers and articles of type II diabetes and fuzzy logic were collected from different sources and research on them assisted on developing the questionnaire required for the survey. A 15-item questionnaire was developed to achieve the aspired study, which is attached in the appendix chapter. The questionnaire included demographic information regarding the patients, the numerical values, the knowledge of the patients regarding type II diabetes etc. The questionnaire was prepared considering the patients whether they are from non-healthcare professions. They were also assured that their personal information would be kept confidential and the participants were mostly relatives of university students who reside in Dhaka. The survey was done between March 2018 and July 2018. The questionnaire used in this survey is attached in the appendix part.

3.3. Methodology of data collection:

We collected the average PPG (postprandial glucose) level of 10 patients. Then, we calculated the lowest, optimum and highest PPG recorded. The lowest, optimum, and highest PPG levels are as following L = 6.5, O = 9 and H = 11.5. Finally, we included the values in a table labeled as F1. The PPG levels of 10 patients in F1 table include 6.5, 8.00, 8.00, 10.00, 9.00, 7.00, 10.00, 10.00, 11.00, and 7.00. So, the L (low) = 6.5, O (optimum) = (6.5+11.5/2= 9.00) and H (high) = 11.5. Secondly, we collected the duration, for how many years the patient is on insulin, of 10 patients. Then, we calculated the lowest, optimum and highest duration recorded. The lowest, optimum, and highest durations are as following L = 1, O = 14 and H = 27. Finally, we included the values in a table labeled as F2. The durations for how many years the patients are using insulin of 10 patients in F2 table include 1, 7, 7, 9.8, 18, 2, 2, 6, 27, 11 years respectively. So, the L (low)=1, O (optimum) = (1+27/2= 14) and H (high) = 27. Next, we collected the amount of insulin prescribed to the patients and set a range of the amounts prescribed considering the prescribed doses. The ranges are as following, A= 5-16, B= 14-25, C=23-34, D= 32-43 and E=41-52. Finally, we prepared a decision table. The decisions area taken on the basis of F1 and F2 table ranges.

If a person's F1 and F2 both are low, then the Insulin dose range will be A= 5-16, as his/her PPG level is within normal range and the duration of insulin prescribed is short. If a person's F1is low and F2 is optimum, then the Insulin dose range will be B= 14-25, as his/her PPG level is within normal range and the duration of insulin prescribed is moderate. The frequency can be adjusted. If a person's F1 is low and F2 is high, then the Insulin dose range will be D= 32-43, as his/her PPG level is within normal range and the duration of insulin prescribed is long. The frequency of administering insulin can be adjusted accordingly. If a person's F1 is optimum and F2 is low, then the Insulin dose range will be B = 14-25, as his/her PPG level is slightly higher but the duration of insulin prescribed is short. If a person's F1 and F2 both are optimum, then the Insulin dose range will be D= 32-43, as his/her PPG level is on borderline and the duration of insulin prescribed is moderate. The frequency of administering insulin can be adjusted accordingly. If a person's F1 is optimum and F2 is high, then the Insulin dose range will be E= 41-52, as his/her PPG level is above the normal range and the duration of insulin prescribed is long. The frequency of administering insulin can be adjusted accordingly.

If a person's F1 is high and F2 is low, then the Insulin dose range will be F= 25-36, as his/her PPG level is very higher. Though the patient's duration of insulin prescribed is short, he/she should be prescribed on the initial stage to control the increase. If a person's F1 is high and F2 is optimum, then the insulin dose range will be F= 25-36, as his/her PPG level is on borderline and the duration of insulin prescribed is long. The frequency of administering insulin can be adjusted accordingly. If a person's F1 and F2 both high, then the Insulin dose range will be E= 41-52, as his/her PPG level is above the normal range and the duration of insulin prescribed is long. The frequency of administering insulin can be adjusted accordingly.

3.4. Methodology for using MATLAB:

3.4.1. Computer Process Interfacing:

A troupe of hardware and software is called interface, which can be used in a malleable way and is able to process instrument to a digital computer. Differential equations are used to describe the analogue signals of plant and process. On other hand, digital computation is explained by such equations. Digital computation is basically is discrete spectra of digital signals. In case of production of digital controllers or intelligent instruments, the interrelation between these two aspects is very important. The following figure resembles the signal flowing from a plant to a digital computer and reversing back to the plant. (Besta et al., 2013)

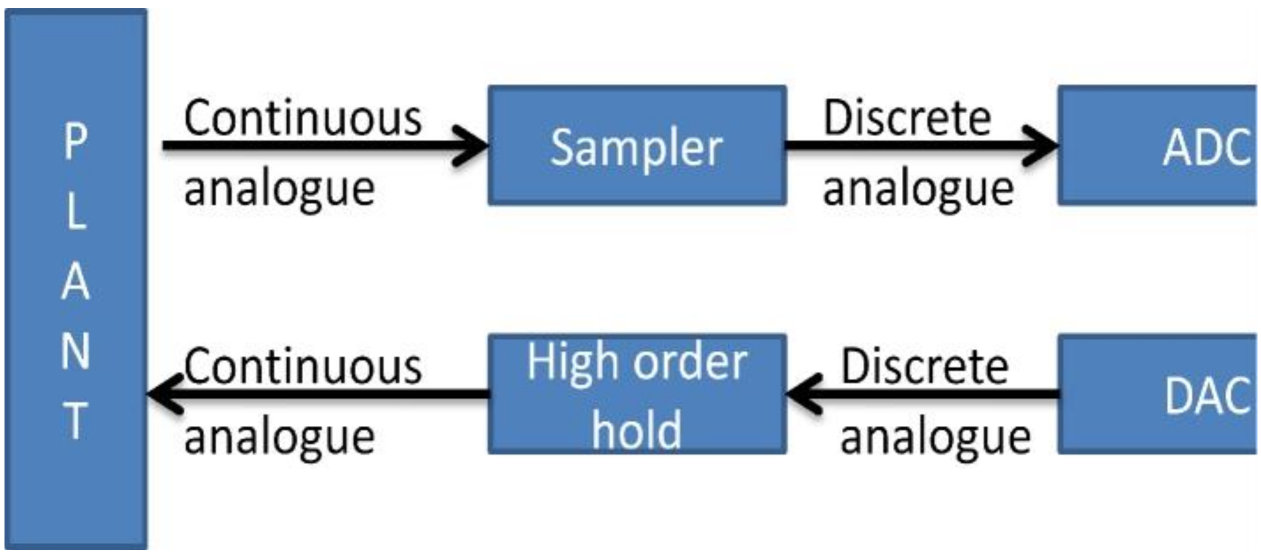

Figure 3.1: Flow of Signal to the Computer from the Plant (Besta et al., 2013)

3.4.2. Real-time Applications using MATLAB:

MATLAB; software, that helps hardware (digital computer) to wield data according to the preordained guidance. The real time applications using MATLAB are shown below:

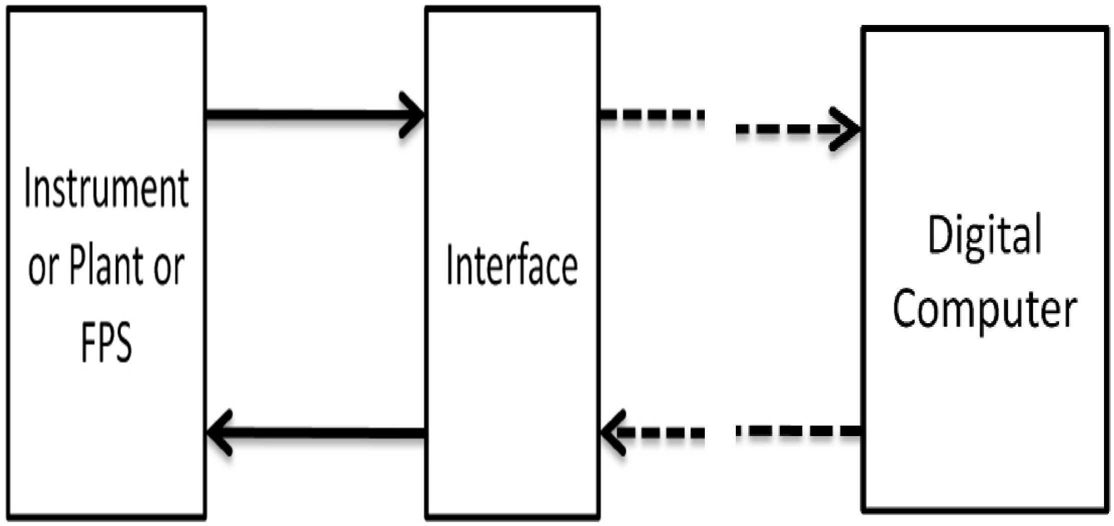

Figure 3.2: A Real-Time System and its Parts (Besta et al., 2013)

3.4.3. Fuzzy Logic Control Technique

Formal translation of imprecise human decisions into composed and disciplined strategies is proffered by Fuzzy logic. It facilitates efficiency through the profiteering. Fuzzy logic can be can be beneficial in process control. The variables for the process need to be deliberate and the system, which needs to be amplified, should be developed. The fuzzy logic was built with the concept of input and output of data. A study and investigation of a fuzzy logic model that performed well for the wide operating ranges considered that it can be used with confidence for the online control. The obtained results showed an effective control of state variables in distillation plant. (Besta et al., 2013) The in-built software of MATLAB Script comprises of three sections: a) Input section, b) Output section, and c) Control section. (Besta et al., 2013)

3.4.4 Flow process of fuzzy control design:

Fuzzy logic designing demands the mastery over the controlled process. Fuzzy logic controller involves the following trail-

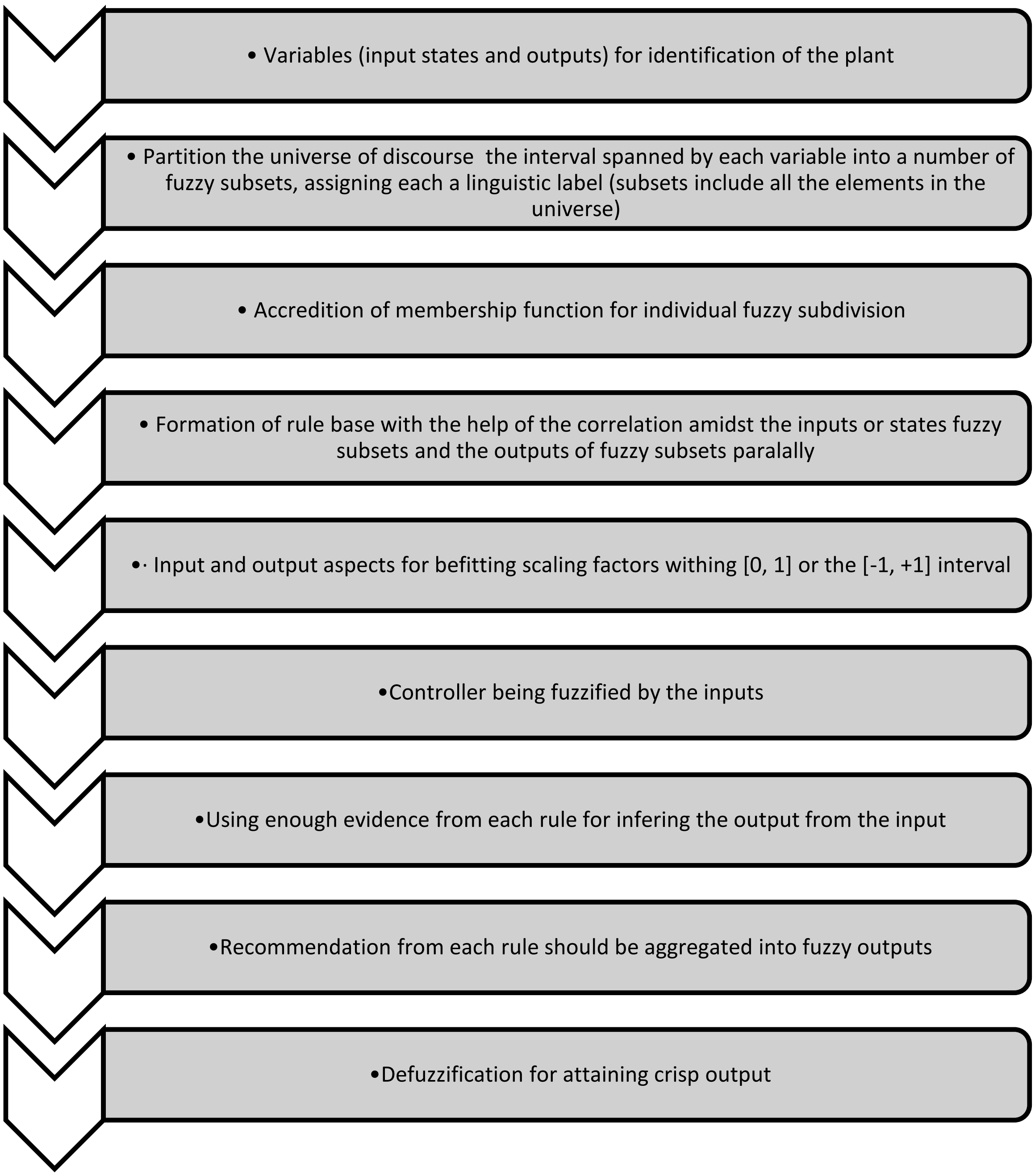

Figure 3.3: Flow process design (Besta et al., 2013)

During the fuzzification step, the Flow and flow rates are chosen as input variables, which are divided into three fuzzy sets and named as HIGH, LOW and OK as shown in the following figure-

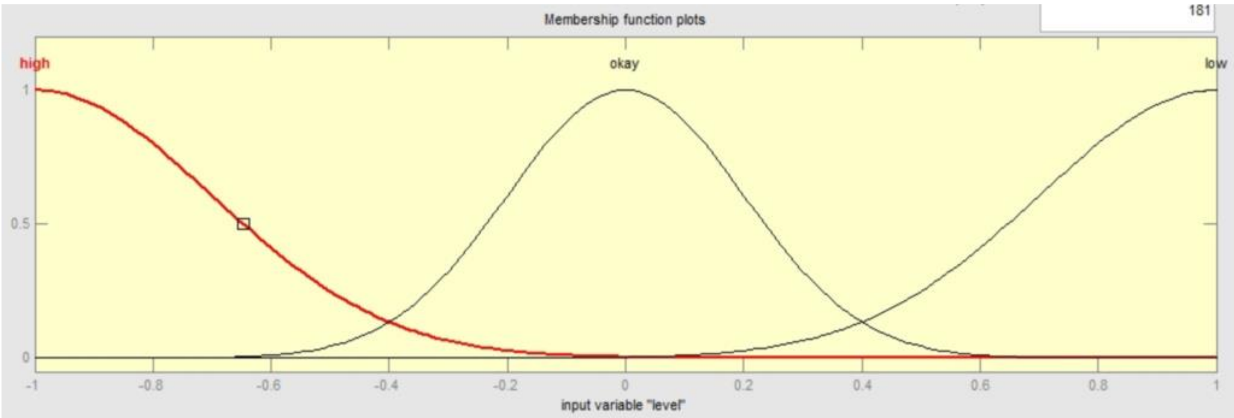

Figure 3.4: Error of Input Membership Function (Besta et al., 2013)

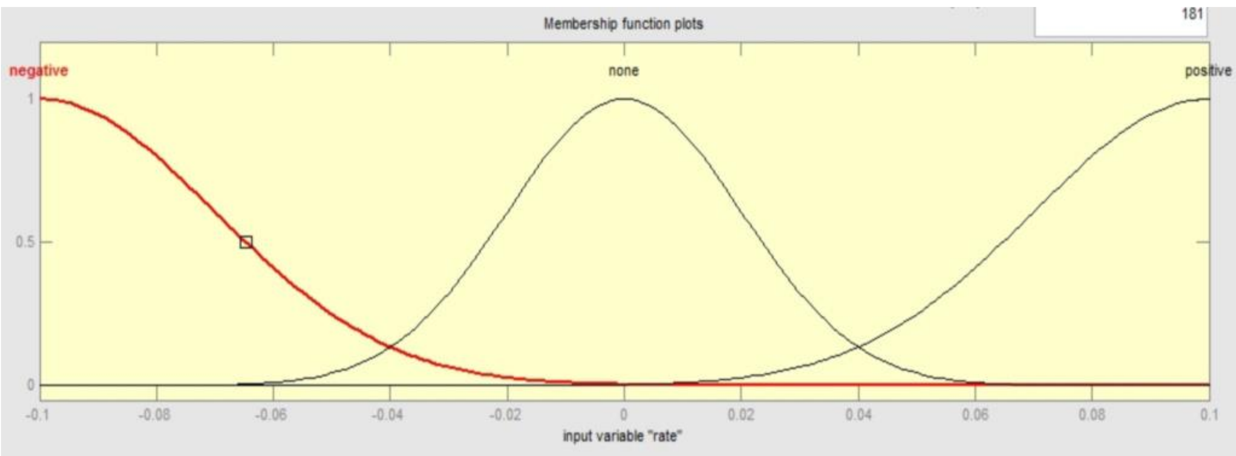

Figure 3.5: Error during Change in Input Membership Function (Besta et al., 2013)

3.4.5. Methodology for using MATLAB in designing insulin dose:

In the beginning we have set post prandial glucose level and duration of receiving insulin treatment as inputs so that we could get a precise insulin dose as output. For postprandial glucose level (F1) the ranges include L (6, 7, 8), O (8, 9, 10) and H (10, 11, 12).

Table 3.1: Input of Postprandial Glucose Level

F1 ranges	
Category	**Range**
L	6-8
O	8-10
H	10-12

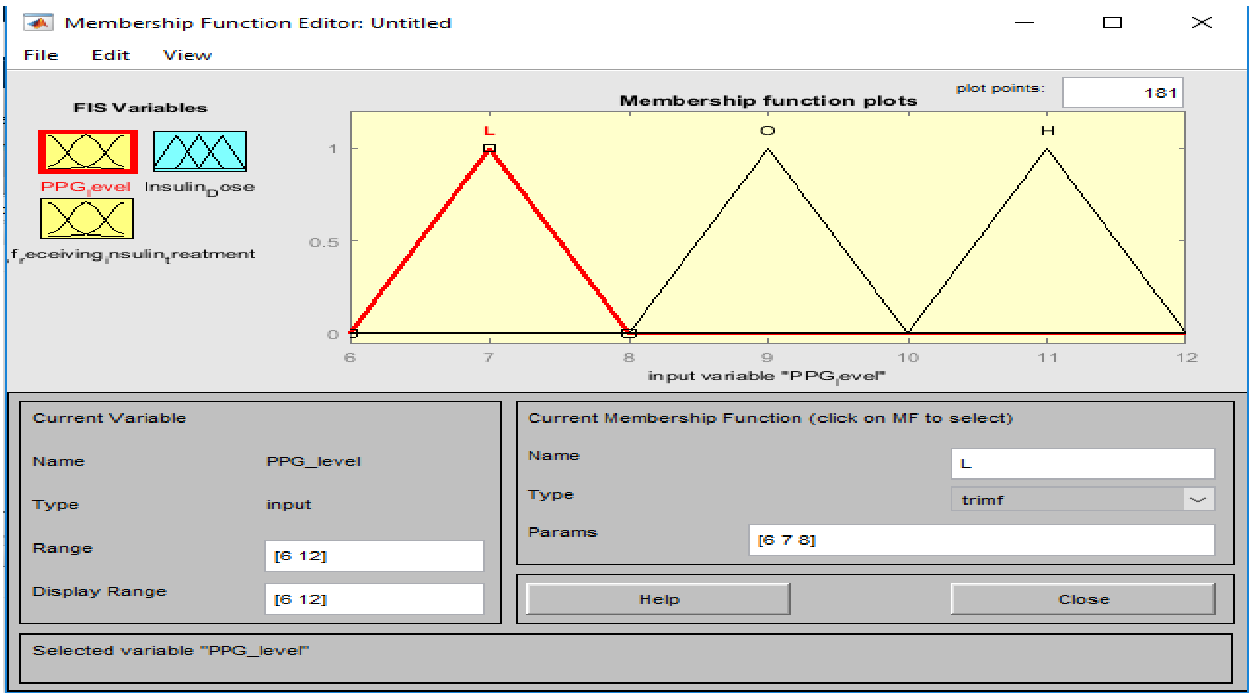

Figure 3.6: Graph of Input of Postprandial Glucose Level

For duration of receiving insulin treatment (F2) the ranges include L(1, 5.5, 10),O(10, 14.5, 19) and H(19, 23.5, 28).

Table 3.2: Input of Duration of Receiving Insulin Treatment

F2 ranges	
Category	**Range**
L	1-10
O	10-19
H	19-28

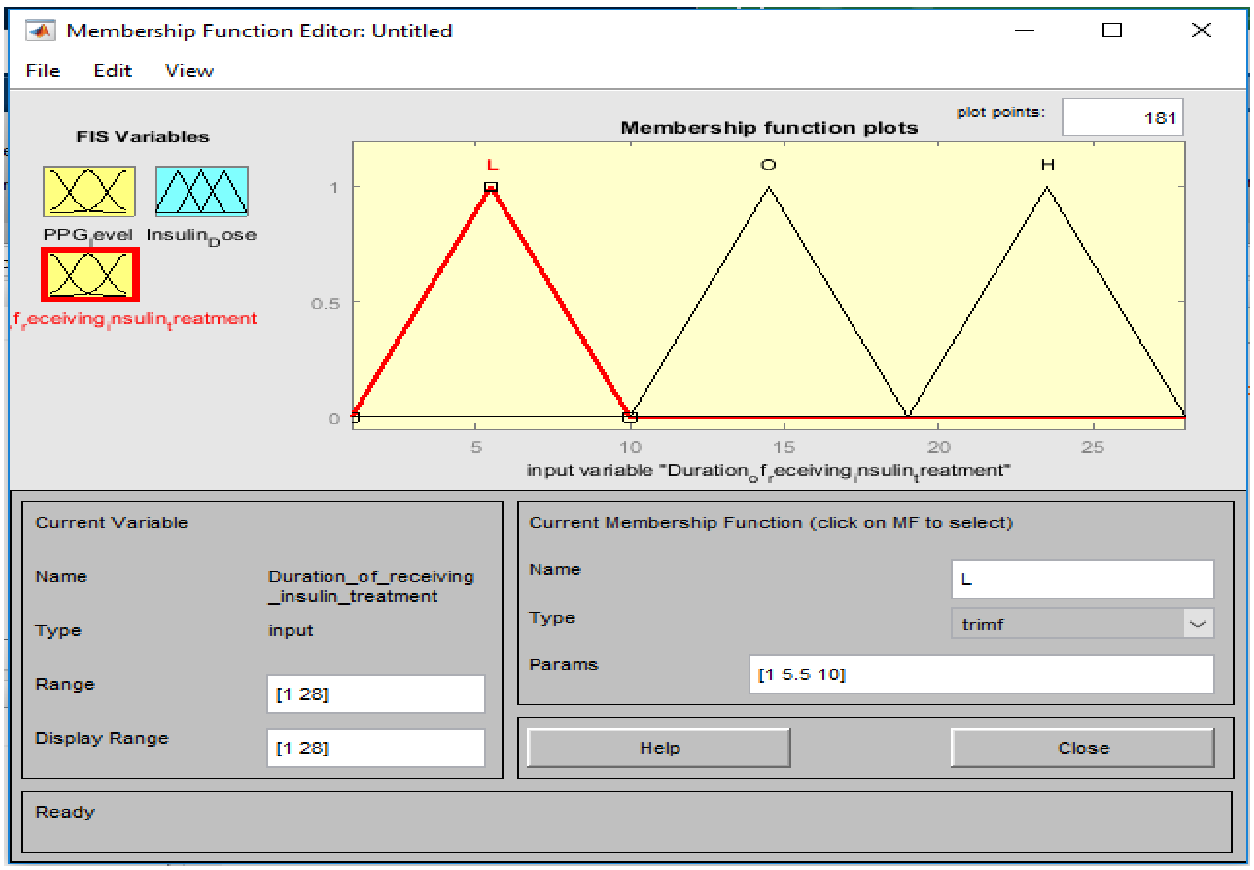

Figure 3.7: Graph for Input of Duration of Receiving Insulin Therapy

Similarly, divided the insulin dose within ranges A(5, 10.5, 16),B(14, 19.5, 25),C(23, 28.5, 34),D(32, 37.5, 43),E(41, 46.5, 52) and F(25, 30.5, 36). The values were divided within ranges to exclude any overlap or discontinuation in the curve. The value F was introduced to include the deviated values that do not directly fall under the ranges of values mentioned in A to E.

Table 3.3: Input of Prescribed Insulin Dose

F1 ranges	
Category	**Range**
A	5-16
B	14-25
C	23-34
D	32-43
E	41-52
F	25-36

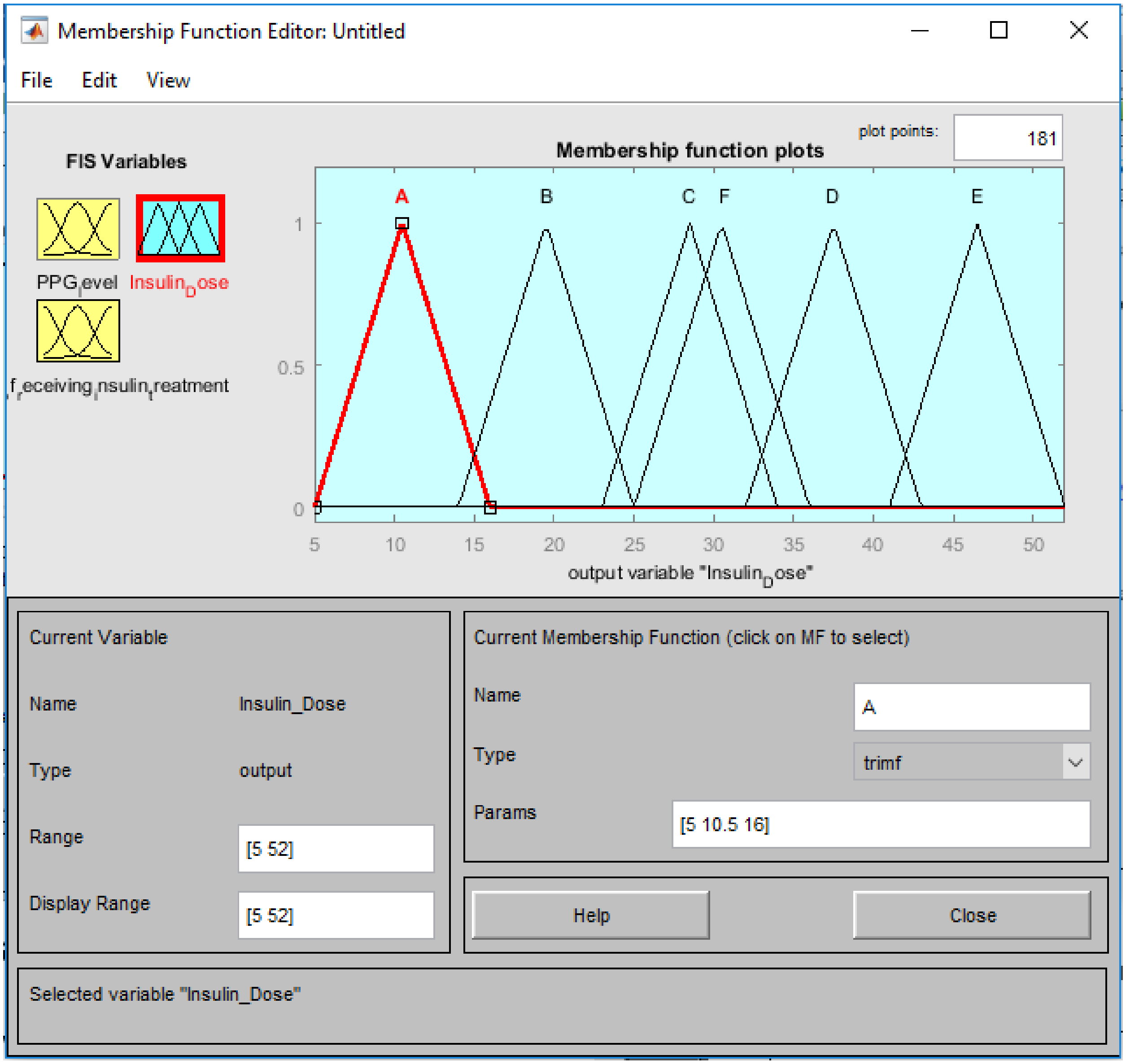

Figure 3.8: Graph of Output.

After giving input of the numerical values, we set 9 rules, which are recognized as IF-THEN rules to observe the surface diagram. The IF-THEN rules are as following:

- If PPG level is low (L) and duration of receiving insulin treatment is low (L) then insulin dosage is A.
- If PPG level is low (L) and duration of receiving insulin treatment is optimum (O) then insulin dosage is B.

- If PPG level is Low (L) and duration of receiving insulin treatment is high (H) then insulin dosage is D.
- If PPG level is optimum (O) and duration of receiving insulin treatment is low (L) then insulin dosage is B.
- If PPG level is optimum (O) and duration of receiving insulin treatment is optimum (O) then insulin dosage is D.
- If PPG level is optimum (O) and duration of receiving insulin treatment is high (H) then insulin dosage is F
- If PPG level is high (H) and duration of receiving insulin treatment is low (L) then insulin dosage is F.
- If PPG level is high (H) and duration of receiving insulin treatment is optimum (O) then insulin dosage is D.
- If PPG level is high (H) and duration of receiving insulin treatment is low (H) then insulin dosage is E.

The rules are actually based on the human decisions, which were taken on the basis of PPG level and duration of receiving insulin treatment. So, based on the blood sugar concentration after meal and the duration of taking insulin are the main criteria that help to input some decisions. For example, if a person has a high PPG level and he or she has been taking insulin for a prolonged period then his insulin dosage is E. E ranges between 41 to 52.

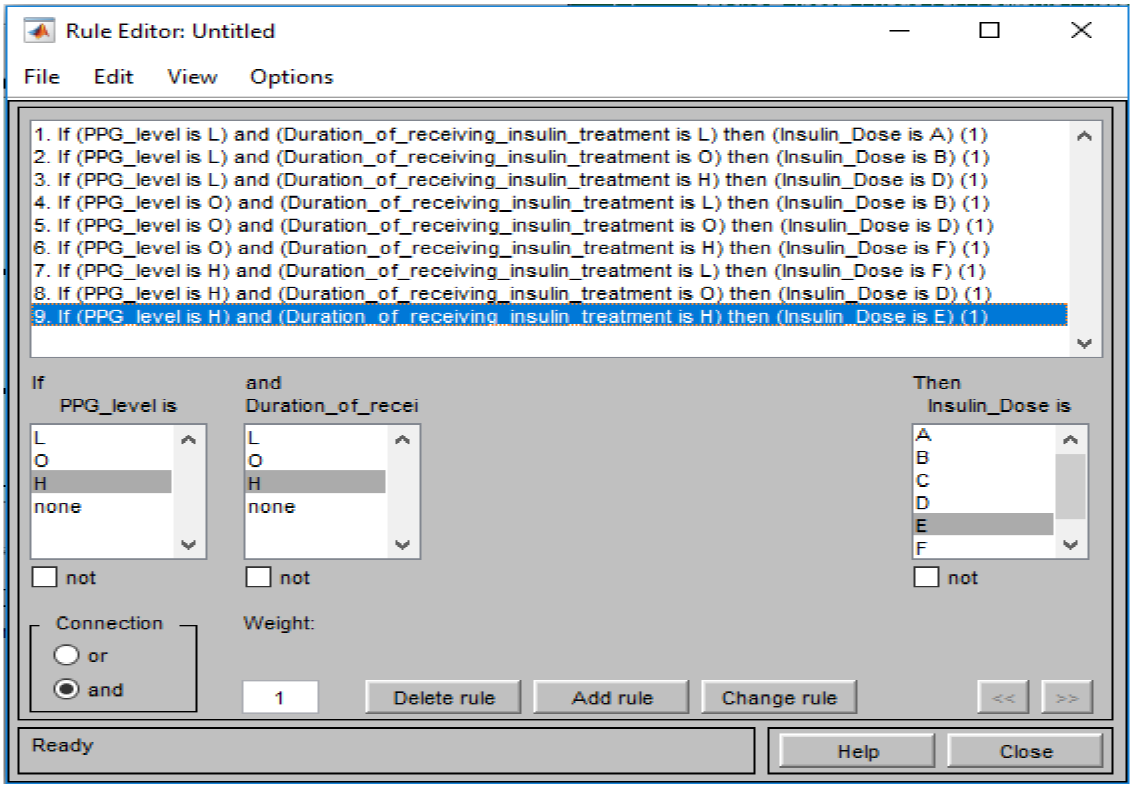

Figure 3.9: IF-THEN rule

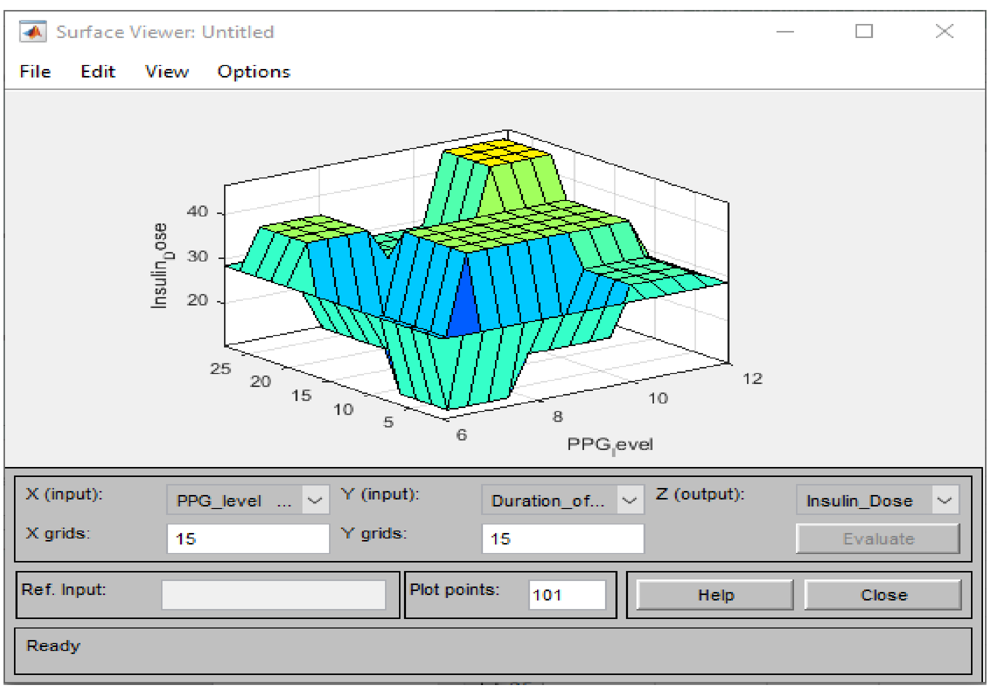

Figure 3.10: Graphical Representation of the Values

3.4.6. De-fuzzification:

The last step of this process is called de-fuzzification which involves the process of returning crisp value as output. Different methods of de-fuzzification are available in MATLAB. Here, we have used the "centroid" method. The reason of selecting this method is getting approximate results for the subject under consideration. At the end of this process a crisp number regarding insulin dosage is achieved.

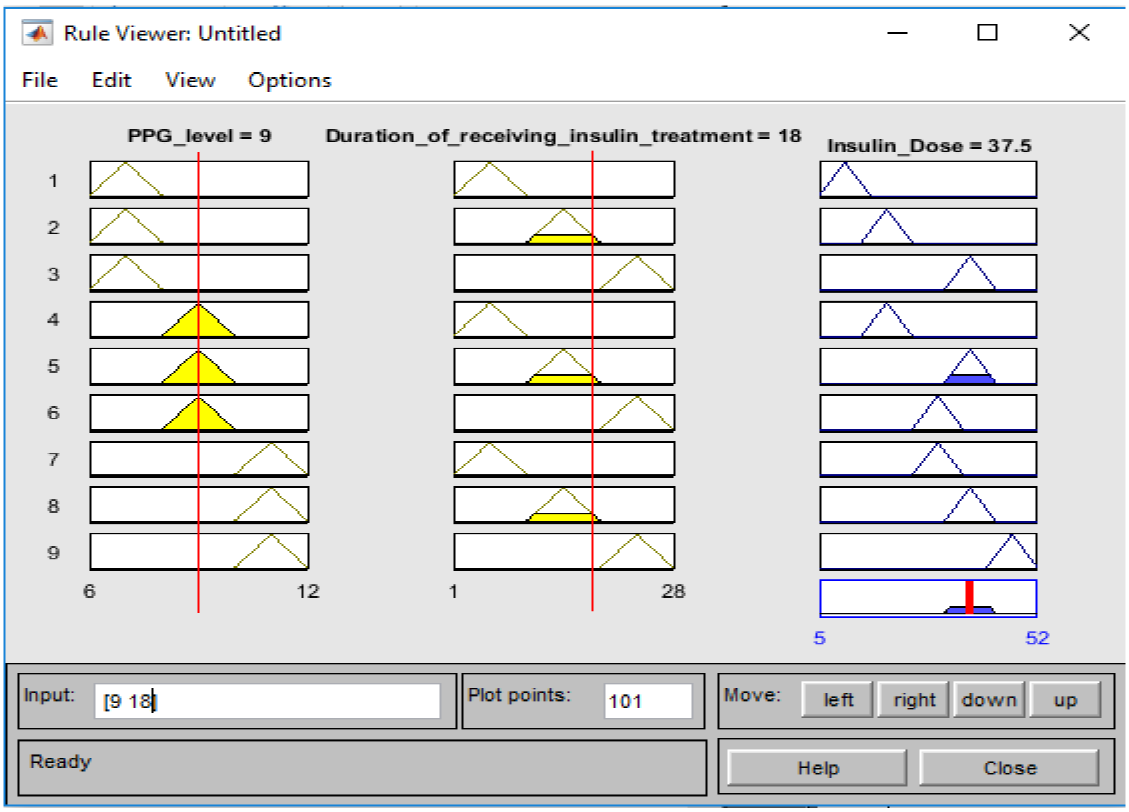

Figure 3.11.1: Insulin Dosage Derived Using FL in a Patient (Male).

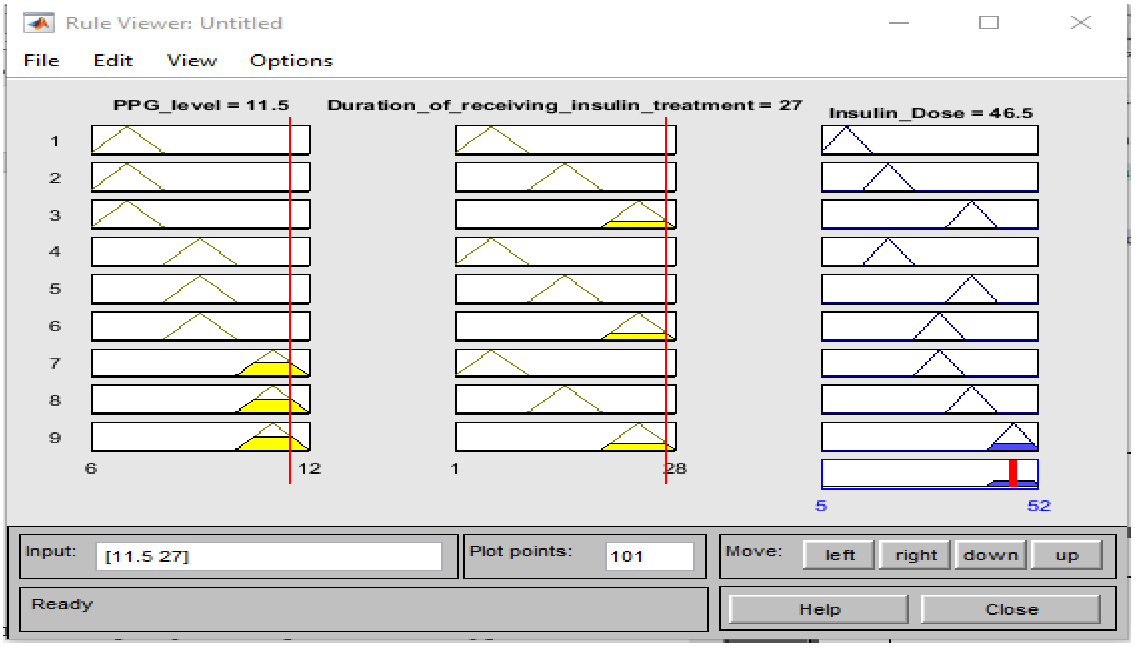

Figure 3.11.2: Insulin Dosage Derived Using FL for an Adult Patient (Female)

Table 3.4: Defuzzification

Chapter IV

4. Result and Discussion:

As mentioned earlier, the survey was conducted on people with type II diabetes. For ease of calculation, data of 10 randomly selected patients were used in this study. The patients were provided with a questionnaire, which is attached in the appendix part and asked to fill out some specific information. The ratio of male to female patients was 70% and 30%. The participants were from different educational and social background. Some of them were very cooperative and enthusiastic about the study; whereas, some were concerned about the confidentiality of this research. A large population of this survey was on people from non-medical background, who were not able to answer all the questions properly. Nearly, 33% people were able to fill up the whole questionnaire correctly. Some contributors were partially correct about some questions as an example, when they were asked about how many times they take insulin, some answered 0 times; whereas, the study is for who takes insulin.

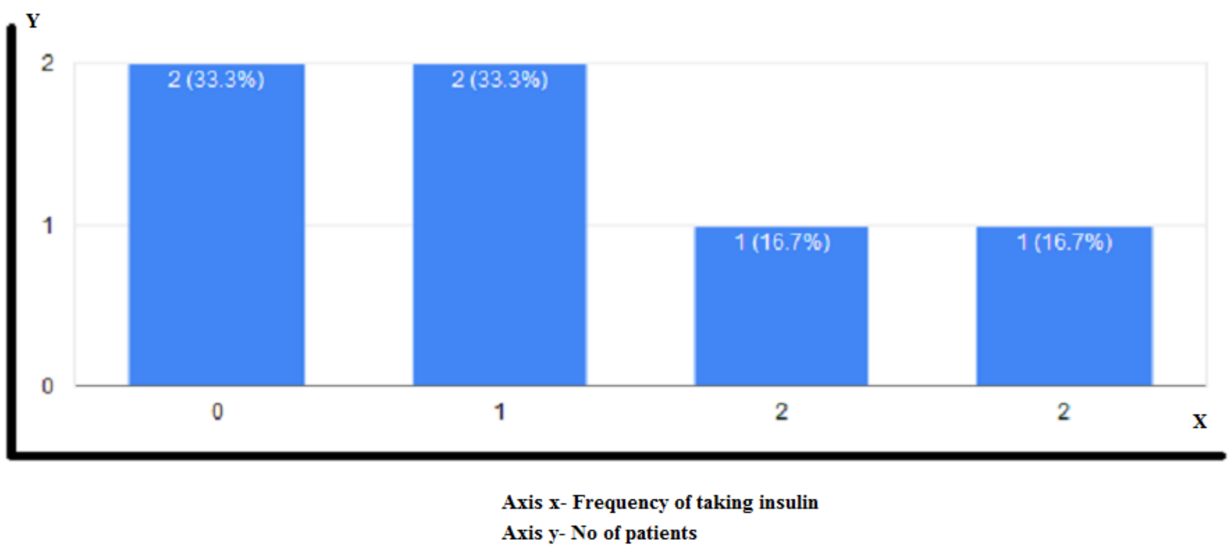

Figure 4.1: Frequency of Taking Insulin of the Participants.

They were also asked relevant questions apart from core questions of this study such as the amount of insulin they take daily, their PPG level and the duration of receiving insulin treatment to introduce and make them comfortable with the survey. They were asked about their family history of diabetes, being on any oral medications for better glycemic control, maintaining any special diet or exercise regimen for better hold over blood glucose level or any sudden incidence of increase or decrease in blood sugar concentration. The patients were mostly accurate while answering these questions. Almost 77.80% of the patients have a family history of diabetes. 66.70% are recommended to follow special diet or exercise regimen for better glycemic control and 22.20% had a recent incidence of exacerbation or alleviation of blood sugar concentrations.

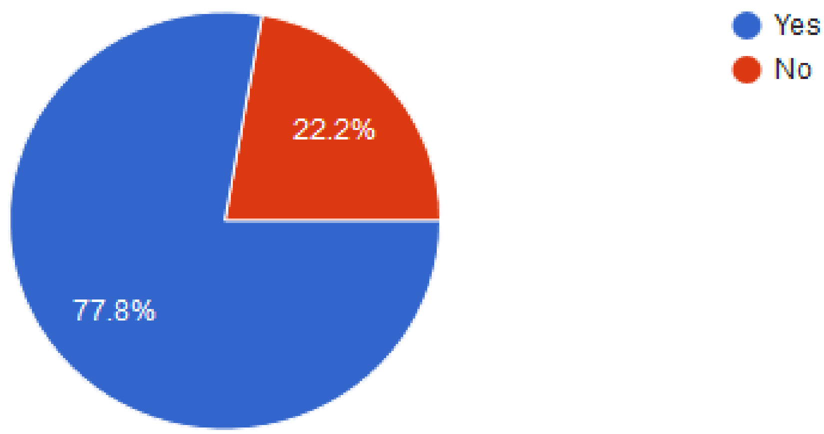

Figure 4.2: Family History of Diabetes in Type II Diabetes Patients.

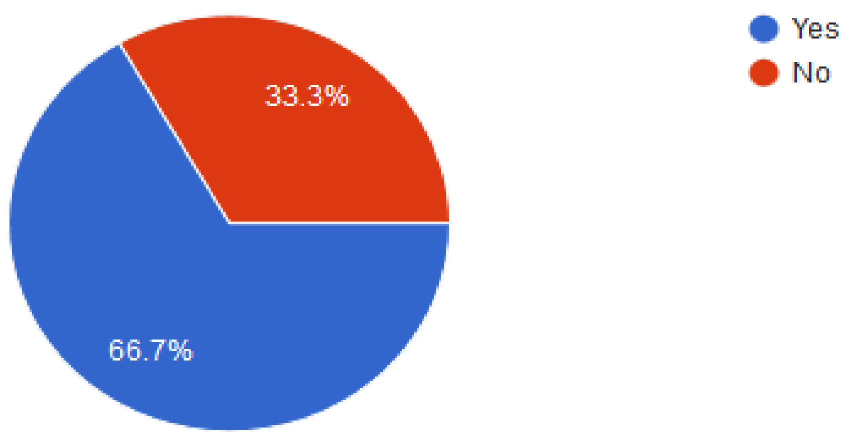

Figure 4.3: Participants with Recommendations for diet and exercise regimen

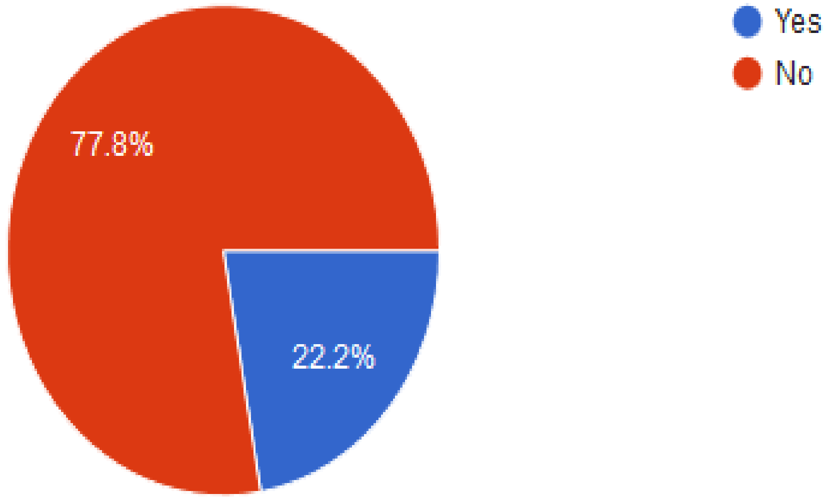

Figure 4.4: Recent Increase in Blood Glucose Level of the Participants

After the survey was done, the data that was collected were analyzed. On the next step, the PPG levels were opted and three ranges L (low), M (Medium) and H (high) was set. Then the values of PPG were set in the table. The same was done with the values of duration of receiving insulin treatment and prescribed insulin dose. Based on these numerical magnitudes a human decision table was prepared regarding the insulin dose. Depending on this, building fuzzy logic was done with the help of MATLAB. Finally, the desired dose of insulin was achieved. All these steps are briefly discussed in the methodology part. The comparison of obtained dose and the prescribed dose is done in the following table.

Table 4.1: Comparison between the Physicians's Prescribed Dose and the Obtained Dose

Pt No.	**Average PPG level**	**Duration of receiving insulin therapy**	**Physician's prescribed insulin dose**	**Predicted insulin dose**
1.	6.5	1.0	14	28.50
2.	8.0	7.0	12	28.50
3.	8.0	7.0	10	28.50
4.	10.0	9.8	40	28.50
5.	9.0	18.0	34	37.50
6.	7.0	2.0	18	10.50
7.	10.0	20.0	40	28.50
8.	7.0	6.0	17	10.50
9.	11.5	27.0	50	46.50
10.	7.0	11.0	14	19.50

In the table, the difference between the physicians prescribed insulin dose and attained insulin dose is observed. As a fact of example, a subject with a postprandial glucose level of 9 mg/dl and who has been receiving insulin therapy for 18 years, the insulin dosage for the patient will be 37.5 units. His prescribed insulin dose by his physician was 37.5 units. Therefore, the neat difference in insulin dose prescribed by the physician and the insulin dose derived using fuzzy logic is 3.5 units. If we see another patient as an example, whose PPG level is 11.5 mg/dl and who has been taking insulin for 27 years. The insulin dosage will be 46.5 units for that person. On the other hand, he was recommended to take 50 units of insulin by the doctor. To add more, her insulin dosage achieved in fuzzy logic is less than the amount of insulin prescribed for that patient.

Chapter-V

5. Drawbacks and Challenges:

This research is not unlike other research based studies. It has its own drawbacks, which is required to be addressed. For example, in table 4.1, there are some obtained insulin dose using MATLAB, which is significantly different from the prescribed dose and there can be several possible reason for this. The patients could have provided wrong information due to lack of proper knowledge. This also could be due to the patient's not taking the insulin dose properly or not maintaining a healthy lifestyle. The presence of another disease or being on any other medications could also be the possible causes of such deviation. On the other hand, the results that have been obtained can also not be completely accurate, as this has not been applied due to not having the authority to prescribe insulin dose to patients. During conduction of the survey, situations like participants being from non-medical background or belonging to different social status were a bit crucial to handle. Also, pursuing them to share the information and assuring about the confidentiality was challenging.

Chapter-VI

6. Future Scope:

The future scope of using artificial intelligence is imminent in designing drug dose. AI has been used in field of health science and medicine due to its applicable, practical and inevitable use.(Miller & Brown, 2018) There are so many possibilities. If pharmacists and doctors work hand in hand and if this project can be collaborated, then it is possible to design better drug dosage for the patients. As, pharmacists have the expertise of designing accurate dose for a patient considering his or her physiological parameters and doctors have the authority to prescribe drug to patients, it can benefit the humanity .

Chapter VII

7. Conclusion:

Different studies have derived to a conclusion that majority of the patients with type 2 diabetes failed to attain and maintain optimum glycemic control worldwide. (Selim, 2017) This information inspired to conduct this research to design a method of getting more decisive dose of insulin for the patients with type II diabetes. It gives more personalized calculations of insulin dose. (Chowdhury, Khan, Nirzhor, Jabin, & Islam, 2017) In this study, different types of values were observed and these indicated towards the probability of precise dose as the dose was designed considering different factors. Some of the results were close and some were distant from the prescribed dose of insulin, which can be used for furthermore studies and research to utilize and get the best possible outcomes.

Chapter VIII

8. Appendix:

Dear Sir/Madam,

We are conducting a survey to understand the correlation of average blood glucose level before and after meal with daily insulin dosage. In this questionnaire, we are particularly collecting information regarding diabetes management.

Please answer the following questions as instructed. We assure you that the information you provide will be used for the purposes of this study only.

No of ques.	Questions	Responses
1.	Do you have a family history of diabetes?	○ Yes ○ No
2.	What is the amount of insulin units you are prescribed per day?	
3.	How many times you are supposed to take the insulin in a day?	
4.	Do you monitor your blood sugar regularly?	○ Yes ○ No
5.	If yes, then what is your average blood glucose before and after meals?	
6.	If no, what is your current blood glucose level? (last 5 days)	
7.	Are you on any oral medication for diabetes?	○ Yes

		○ No
8.	If yes, then what are the names of the medication you take for diabetes?	
9.	Are you diagnosed with any other disease?	○ Yes ○ No
10.	If yes, then what are the names of the diseases?	
11.	Are you currently on any other medication?	○ Yes ○ No
12.	If yes, then what are the names of the medications?	
13.	Are you recommended to follow any special diet or exercise regimen?	○ Yes ○ No
14.	Is there any recent incidence of sudden increase or decrease of your blood sugar level?	
15.	If yes, then on a scale of 1-10 how would you like to rate the severity of the incident? (1 being least severe and 10 being most severe)	

Chapter IX

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