Fuzzy Logic: A Contemporary Technique in Refining Physicians' Prescribed Total Daily Insulin Dosage for Type 2 Diabetes Patients

A project submitted

by

Md. Tariqul Islam Tareq

ID 13346040

Batch: Summer 2013

to

The Department of Pharmacy

in partial fulfillment of the requirements for the degree of

Bachelor of Pharmacy (Hons.)

Inspiring Excellence

BRAC University

Dhaka, Bangladesh

September 2018

Dedicated to my family members for their endless support

Certification Statement

This is to certify that this project titled 'Fuzzy Logic: A Contemporary Technique in Refining Physicians' Prescribed Total Daily Insulin Dosage for Type 2 Diabetes Patients.' submitted for the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy, BRAC University constitutes my own work under the supervision of Saif Shahriar Rahman, Senior Lecturer of Department of Pharmacy, BRAC University and that appropriate credit is given where I have used the language, ideas or writings of another.

Signed,

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Countersigned by the supervisor,

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Acknowledgement

I would like to begin by thanking Almighty Allah (SWT.) for granting me the strength to have come this far.

Next, I would love to express my heartfelt appreciation and gratitude to my supervisor, Saif Shahriar Rahman, Senior Lecturer of Department of Pharmacy, BRAC University, for his constant motivation and endless efforts throughout my project. He has thoroughly guided me and opened my eyes to the concept of Artificial Intelligence and its endless applications in the field of medical sciences. For his continuous support, effort and feedback in this project, I will be eternally grateful.

In addition, I would like to thank Prof. Nazmun Nahar, Director General, BIRDEM (Bangladesh Institute of Research and Rehabilitation for Diabetes) and Prof. M Hasnat, Chairman, Department of Endocrinology, BSMMU (Bangabandhu Sheikh Mujib Medical University) for granting me the permission to have access to all relevant inpatient data and interaction, therefore enabling the survey a tremendous success.

I would like to acknowledge and express my heartiest thank to Rubayat Islam Khan, Senior Lecturer of Department of Pharmacy, BRAC University and Ahmed Masud Chowdhury for their guidance and assistance with the relevant data software tool, crucial for the completion of this project.

Furthermore, I want to thank my fellow mate, Proma Roy Orni for her continuous presence and help in every step of this entire project. Without her presence, assistance in patient interaction and data mining, this project would not achieve succession.

Last but never the least; I would like to wholeheartedly thank my family and my friends for being a blessing and a continuous support throughout my undergraduate career.

Abstract

Type 2 diabetes mellitus (T2DM) is one of the major global health challenges across the world with an elevated prevalence rate worldwide and responsible for 90-95% of total diabetes cases. The management of T2DM depends on conventional insulin therapy that does not have the ability to perfectly provide accurate glucose regulation inside the body. In a conventional insulin therapy, physicians prescribe insulin dosage for the patients by taking into account patient-related factors (PRFs) i.e. weight, height, BMI or carbohydrate intake discretely or considering only one factor. The succession of insulin dosage depends on the close consideration of all the factors that have a positive correlation with the insulin sensitivity. Thus traditional insulin therapy, in turn, causes instances of hypoglycemia and hyperglycemia among the vast number of diabetes patients. This project examined 24 randomly selected T2DM patients admitted into two hospitals of Dhaka city through utilization of a fuzzy logic based technique to further tune the physicians' prescribed total daily insulin dosage for alleviating the hypoglycemic and hyperglycemic incidences among these patients. Two patient-related factors (PRFs) such as-average fasting blood glucose level (AFBGL) and average daily protein intake (ADPI) were considered as inputs for the fuzzy-logic system as these two PRFs have a positive correlation with insulin sensitivity. After considering insulin dose as an output variable, appropriate membership functions were defined by using MATLAB Fuzzy Logic Designer Toolbox. Furthermore, to establish a relationship among the membership functions, the 'if/then rules' are then set in the interface that also provides the fuzzy system with a decision-making facility. The last process known as defuzzification has enlightened the project by generating an output known to as predicted insulin dose (PID) as a recommendation by the fuzzy-based system for each patient. Through a quantitative comparison between the predicted insulin dose (PID) by the fuzzy system with the physicians' prescribed insulin dose (PPD) for every patient, a numerical difference of different degrees was obtained indicating an additional or reduced administration of insulin dose by the patient so far causing the critical events (hyperglycemia & hypoglycemia) more prominent in their everyday life. The result of this experiment is further evinced by the data collected from those two hospitals where the experimented patients were admitted. Our experimental findings have shown a number of previous hyperglycemic and hypoglycemic events experienced by the patients as predicted by the fuzzy system respectively. Accordingly,

the predicted insulin dose by the fuzzy system is believed to alleviate the hypoglycemic and hyperglycemic events in these patients in the future. Finally, a low mortality rate and a beneficial financial condition followed by a better quality of life for these 24 type 2 diabetes mellitus (T2DM) patients were possible by utilizing this prominent form of Artificial Intelligence used for precision dosing on insulin.

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List of Acronyms

WHO = World Health Organization

BIRDEM = Bangladesh Institute of Research and Rehabilitation for Diabetes, Endocrine and Metabolic Disorders

BSMMU = Bangabandhu Sheikh Mujib Medical University

T2DM = Type 2 Diabetes Mellitus

PRF = Patient Related Factor

FBGL = Fasting Blood Glucose Level

AFBGL = Average Fasting Blood Glucose Level

ADPI = Average Daily Protein Intake

mmol/L = Milimoles per Liter

USDA = United States Department of Agriculture

MF = Membership Function

PID = Predicted Insulin Dose

PPD = Prescribed Insulin Dose

HBS = High Blood Sugar

LBS = Low Blood Sugar

Chapter 1

Introduction

Diabetes is a leading global health problem that has affected over 422 million adults, and is responsible for 5.3 million deaths in 2013 (WHO, 2016; Mahbub, 2016). Compared to the 1980s, the rate of prevalence has increased now from 4.7% to 8.5% in the adult population globally, markedly in the low- and middle-income countries (WHO, 2016). Notably, a study on 15016 people registered in the year of 2000 at Bangladesh Institute of Research and Rehabilitation for Diabetes, Endocrine and Metabolic Disorders (BIRDEM) in Bangladesh showed a higher prevalence rate among the population of urban/semi-urban areas in comparison to rural areas (Imam & Hossain, 2012). Its proportional mortality is 3% of total deaths in all ages population of Bangladesh (World Health Organization, 2011). WHO also states that the percentage of adult people living with overweight, obesity, and physical inactivity in Bangladesh are 17%, 3.3%, and 25.1 % respectively. These are the most contributing risk factors for diabetes that has long-term complications on different organs of the human body. It is estimated that among the total number of people reported a blindness and vision impairment due to diabetic retinopathy around the world, 51% and 56% are those from the Asia-Pacific respectively (Chua, Lim, Wong, & Sabanayagam, 2018). Currently, about one in ten Bangladeshi adults have diabetes (WHO, 2016). Moreover, it is suggested that the number of affected people will rise to 592 million globally by 2035 and 11.12 million alone in Bangladesh by 2030 (Rahman et al., 2015; World Health Organization, 2011).

Diabetes mellitus is a metabolic condition that is characterized by chronic hyperglycemia due to the deficient activity of insulin inside the body (American Diabetes Association, 2010). The fundamental pathophysiological features responsible for the insufficient activity of insulin include- inability to secrete insulin due to autoimmune destruction of the β-cells and/or defective insulin response that comprises poor insulin secretion and reduced tissue reaction to insulin in the complex pathways of hormone action. During food digestion, carbohydrates are broken down to glucose; the energy source of the human body. Glucose is then transported to various organs of the body by the bloodstream. Insulin is the hormone produced by the beta cells of the pancreas and is necessary for glucose intake by target cells. In a healthy human body, insulin binds to its receptor after their production from the pancreas. This opens the channels through which glucose enters into the cell. During the events of the inability to insulin secretion and/or abnormal insulin response, glucose cannot get into the cells that results in an elevated level of glucose in the body, referred to as diabetes mellitus in general. The majority of the cases of diabetes falls into two broad classes - type 1 and type 2 diabetes (American Diabetes Association, 2010).There are two other classes of diabetes- gestational diabetes and pre-diabetes. The etiologic classification of diabetes further identifies other specific types of diabetes such as - genetic defects of β -cell or chemical-induced, infections, uncommon forms of immune-mediated diabetes and other genetic syndromes sometimes associated with diabetes (American Diabetes Association, 2010). Type 1 diabetes is further classified as Immune-mediated diabetes and Idiopathic diabetes, which are insulin dependent diabetes or juvenile-onset diabetes and diabetes of unknown origin respectively (The expert committee on the diagnosis and classification of diabetes mellitus , 1997). It is evident that children and young adults are more prone to get type 1 or Immune-mediated diabetes. This type of diabetes exerts its symptoms when approximately 90% of total insulin-producing beta cells get destroyed. The symptoms include - weight loss, increased thirst, extreme fatigue, increased urination, blurred vision and constant hunger. Type 2 diabetes is the class of diabetes that covers approximately 90–95% of cases of overall diabetes cases (American Diabetes Association, 2010). This form of diabetes can also be referred to as adult-onset diabetes or non–insulin-dependent diabetes. This type of diabetes remains undiagnosed for many years as symptoms come slowly and hyperglycemia develops gradually. It develops in people aged 40 years and above and are most common in people over 55 years ago (Rahim et al., 2002). During the diagnosis of type 2 diabetes, it is observed that the pancreas produces enough insulin, but the body is unable to use that insulin completely (The expert committee on the diagnosis and classification of diabetes mellitus, 1997). This phenomenon is known as insulin resistance. The patient may experience blurred vision, frequent urination, weight loss, nausea, frequent infection, nausea or fatigue and reluctant curing of wounds when affected by this type of diabetes. The possibility of progressing this type of diabetes promotes obesity, lack of physical activity and age. An analysis by the Centers for Disease Control and Prevention in 2014 suggested that gestational diabetes has a prevalence of around 9.2% (DeSisto, Kim, & Sharma, 2014). Gestational diabetes is believed to affect pregnant women, whereas pre-diabetes is an indication where the glycemic variables are more than the normal level but less than the diabetes verge

(American Diabetes Association, 2016; Tabák, Herder, Rathmann, Brunner, & Kivimäki, 2012). During pregnancy, the placenta inside mother's body supports the baby to grow by releasing hormones. However, these hormones make it harder for the mother's body to use the insulin by blocking the action of mother's insulin that causes insulin resistance and thus gestational diabetes takes place (Desisto et al., 2014).

Alleviation of premature mortality and morbidity due to diabetes solely depends on the early diagnosis and proper management of the disease. The longer a person lives with undiagnosed and untreated diabetes, the poorer the health outcomes are likely to be. The early detection of diabetes also aids in reducing the risk factors for cardiovascular disease like – blood pressure and lipid (Herman et al., 2015). The goal of diabetes management is to limit the body glucose to the normal level. The management plan thus includes- following a meal plan, getting regular exercise, and taking medication if required as directed by the physician (Intermountain Healthcare, 2018). In effect, diet and exercise are considered as the cornerstones in the management of type 2 diabetes whereas the patients with type 1 diabetes must inject insulin to survive (Campbell, 2006; Tudor-Locke et al., 2004). A national survey of US diabetic population found that about 66% of all diabetes patient has reported no daily physical activity (Ford & Herman, 1995). Subsequent management of this type of diabetes is done broadly through oral diabetes agents and insulin. Sulfonylureas, Metformin, and Thiazolidinediones are the most common oral agents in treating diabetes. However, patients treated with sulfonylureas face more cardiovascular events according to a study report of the University Group Diabetes Program (Meinert, Knatterud, Prout, & Klimt, 1970). Metformin is the most popular drug of choice for outpatients whereas it exerts most of its contraindications among in patients. With a very little acute adverse effects, thiazolidinediones increase the intravascular volume that is harmful to the patients having a history of CHF (Clement et al., 2004). On the other hand, it does prevent restenosis, the formation of a new blockage in a coronary artery; for why this drug is usually prescribed to the patients with type 2 diabetes who have undergone percutaneous coronary intervention(PCI) (Choi et al., 2004). As these oral agents have limitations for inpatient settings, insulin is the proper choice for management of diabetes for its advantages over oral agents. Then again, the initiation of insulin therapy has some barriers which include – mismanagement in determining insulin dosage, patient annoyance with self-injection, and lack of knowledge regarding new formulations (Thrasher, 2017). It is evident that due to mismanagement in the insulin dosage hyperglycemic and hypoglycemic events are reported (Mayo Clinic, 2017). In fact, a patient-friendly insulin therapy requires a close monitoring on some patient-related factors (PRF) like- weight, body mass index (BMI), average daily carbohydrate & protein intake and physical activity (Chowdhury, Khan, Nirzhor, Jabin, & Khan, 2017). Physicians' prescribe the insulin dosage by considering patient-related factors discretely or sometimes considering only one factor that affects patients' blood glucose level. This trend of prescribing insulin dosage often causes faulty administration of insulin in case of type 2 diabetes (Mayo Clinic, 2017). That in turn leads to problematic insulin dosing which can sometimes be fatal for the patient. Moreover, these general trends of prescribing insulin dosage create a probability of experiencing hypoglycemia or hyperglycemia by the patient as this pathway ignores the values of some other factors those affects patients' blood glucose level. These two adverse events increase morbidity rates in T2DM patients.

Thereupon, it is vital to attain potent insulin dosing to avoid such hyperglycemic and hypoglycemic events where the concept of fuzzy logic comes in. Fuzzy logic is tested as an effective way of achieving exquisite precision in drug dosing because human minds examine approximate data, excerpt meaningful information and exerts crisp solutions (Mahfouf, Abbod, & Linkens, 2001). In this study, we inspected two patient-related factors i.e. fasting blood glucose and daily protein intake in the fuzzy-based system to refine the insulin dosage for type 2 diabetes patient. We hypothesized that fasting blood glucose and dietary protein intake has a positive correlation with insulin sensitivity. Previous studies have shown that, elevated fasting blood glucose level (FBGL) hints β-cell dysfunction which is an intrinsic segment of the pathogenesis of higher blood glucose in type 2 diabetes mellitus (T2DM) patients (Abbasi, Silvers, Viren, & Reaven, 2018; Fabietti, Canonico, Federici, Benedetti, & Sarti, 2006; Hanefeld et al., 2010). This β-cell dysfunction is linked with lower insulin secretion and also associated with a reduced release of islet amyloid polypeptide (IAPP or amylin), that is a newly diagnosed β-cell secretory product (Kahn & Porte, n.d.). In addition, another study performed by considering FBG as one of the inputs in the fuzzy logic based system has also validated its significance in maintaining a normoglycemic state in the patients' physiology by suggesting more accurate insulin dose for each patient (Saha et al., 2018). Likewise, the significance of dietary protein intake in blood glucose level is also scrutinized through research. Even though there exists debate among dietary protein intake and insulin sensitivity, researchers recommend increasing insulin dosage for a high protein diet (Bell, Toschi, Steil, & Wolpert, 2016; Franz, 2000; Nuttall & Gannon, 2013). Information based on these two factors are considered as input variables in the system and rules are developed in MATLAB. Thus, the procedure provides an optimum dosage of insulin as output for the individual patient considering their individual configuration. Through this technique, a more specific and exact insulin dosage has been possible for the individual patient and the possibilities of hyperglycemic and hypoglycemic events in these patients may be defeated in future. Furthermore, this fuzzy logic-based artificial intelligence supports diabetes patients with better quality of life in terms of a precise insulin dosing (Chowdhury et al., 2017; Saha et al., 2018).

Chapter 2

Materials and Methods

2.1. Patients Population

24 randomly selected type 2 diabetes patients were interviewed from Bangabandhu Sheikh Mujib Medical University (BSMMU) & Bangladesh Institute of Research and Rehabilitation for Diabetes, Endocrine and Metabolic Disorders (BIRDEM) both located at Shahbag, Dhaka, Bangladesh. Before that, we got the written permission from the Chairman of Department of Endocrinology, BSMMU and the Director General of BIRDEM to conduct our study over there. Each patient was well informed about the purpose of the study and is strictly consented to its usage.

The patient population comprised of 15 males and 9 females, all of whom were undergoing insulin treatment. The prime aim of the study involves collecting information about their prescribed insulin dosage by the respective physician, fasting blood glucose level and average protein intake per day over a period of 7-10 days. For the purpose of further follow-up, the same patient reported their height, weight, duration of diabetes, average fat intake per day, additional disease complications, detailed treatment plan and answers of some knowledge-based questions to justify their knowledge on their own disease.

4 patients were excluded from the study later, where 2 patients had no information regarding average protein intake per day as they were on IV (Intravenous) saline for the last few days as per their treatment plan by the physician, one due to incomplete interview and other due to wrong information.

2.2. Patient-related factors

2 patient related factors (PRFs) are used as input variables in the fuzzy-based system. These PRFs are – average fasting blood glucose level (AFBGL) and average daily protein intake (ADPI).

2.2.1 Average fasting blood glucose level

As all the patients were admitted into the hospital there had written documents of their daily fasting blood glucose level (FBGL). The registered medical assistants record the fasting blood glucose level of each patient and report those to the physician. For the purpose of this study, 7-10 days fasting blood glucose level were taken as per availability in the hospital database. By using this data, the cumulative average FBGL was then calculated for each patient. The standard unit mmol/L is used in the calculation. According with the observations and recommendations drawn from the studies (Legro et al., 1998; Saha et al., 2018; Silfen et al., 2001) the fuzzy logic membership function was adjusted. Table 2.1 indicates the average fasting blood glucose level of each patient in mmol/L. The table shows that the highest value of average fasting blood glucose level reported by any patient is 18.8 mmol/L, whereas the lowest value is 6 mmol/L reported both by patient No. 12 and 20.

Table 2.1 Average fasting blood glucose level of each patient in mmol/L.

Patient No.	Average fasting blood glucose level (mmol/L)
1.	11.7
2.	10.8
3.	10.2
4.	8.3
5.	12.2
6.	10.5
7.	8.4
8.	8.8
9.	6.9
10.	10.4
11.	10.6
12.	6
13.	10.5

14.	8.4
15.	8.1
16.	9.8
17.	13.6
18.	11.4
19.	18.8
20.	6

2.2.2. Average daily protein intake

The patients reported their daily dietary intake during their ongoing treatment at the hospital. From that diet chart, protein reach foods were identified and dietary protein amount from each food was then calculated by following the publication ‘Nutritive Value of Foods’ which is published by United States Department of Agriculture, USDA (Gebhardt & Thomas, n.d.). From 5 times protein intake each day, the cumulative average daily protein intake of the patient was then calculated. Though protein consumption and its effect on diabetes patients has controversy, research shows almost half of the consumed protein becomes glucose through the process of gluconeogenesis and enters the bloodstream (Franz, 2000). However, data shows that from the dietary protein relatively small amount of glucose enters the circulation (Nuttall & Gannon, 2013). As the high protein diet increases the glucose incremental area under the curve over two-fold, it is recommended to increase the insulin dosage for high protein (>25gm) meal (Bell et al., 2016). Membership function in the fuzzy-based system was fixed as per these findings. Table 2.2 shows the daily dietary protein intake of each patient at different intervals and their cumulative average in gm.

Table 2.2 depicts that among 24 patients, the patient no. 5 has reported the lowest amount of daily dietary protein intake of 30.6 gm. The average daily protein intakes at breakfast, before lunch snacks, at lunch, after lunch snacks and at dinner for this patient were 5 gm, 2 gm, 8.8 gm, 2 gm and 12.8 gm respectively. The table also shows that the highest value of daily dietary protein intake was 98.54 gm that has been reported by patient no. 6. The average daily protein intake by this patient at dinner was 32.72 gm.

Table 2.2 The daily dietary protein intake of each patient at different intervals and their cumulative average in gm.

Patient No.	Average protein intake at breakfast (gm)	Average protein intake before lunch snacks (gm)	Average protein intake at lunch (gm)	Average protein intake after lunch snacks (gm)	Average protein intake at dinner (gm)	Average daily protein intake (gm)
1	7	0	23	4	22.8	56.8
2	14.62	4	30.8	4	9.82	63.24
3	7.8	12	24	4	25.8	73.6
4	9	2	9.6	12	17.3	49.9
5	5	2	8.8	2	12.8	30.6
6	21.82	8	24	12	32.72	98.54
7	3	3	6	4	21.4	37.4
8	9	3	2	0	30	44
9	16	8	17.6	1.1	3	45.7
10	16.8	9.5	20.8	9.5	33.2	89.8
11	20.3	4	24	9	33.7	91
12	13.82	3	23.02	8	19.9	67.74
13	13.5	8	26.02	9	35.22	91.74
14	9.5	12	31.22	9	25.9	87.62
15	5.5	0	21.2	1	4.8	32.5
16	9.8	0	16.2	0	12.8	38.8
17	10	0	23.42	3.4	20.8	57.62
18	16	0	4	0	15	35
19	18.3	12	7	1	29.4	67.7
20	21.3	2	23.02	9	30	85.32

2.3. Computational tool

The programming language MATLAB was used for developing the method and analysis of collected data. A fuzzy-based interface developed in MATLAB was used to calculate the dosage of insulin.

2.3.1 Fuzzification of the membership functions

The input variables of the system are average fasting blood glucose level (AFBGL) and average daily protein intake (ADPI). The output variable is the Insulin Dose (Insulin Dose). The MATLAB Fuzzy Logic Designer Toolbox was used to define the membership function of these inputs and output variables. All these variables consist of various ranges and by using triangular membership functions these input and output variables were fuzzified. The input variables (AFBGL and ADPI) have a membership function with three fuzzy values. These fuzzy values are of different ranges. The different ranges of fuzzy values are - Low (L), Optimum (O) and High (H). On the other hand, the output variable (Insulin Dose) has a membership function with five fuzzy values. These fuzzy values have different ranges too. The ranges of these fuzzy values are A, B, C, D and E. Table 2.3 presents the ranges of the input and output variables. The ranges sets for input variables are 6-19 for average fasting blood glucose level (AFBGL) and 30-100 for average daily protein intake (ADPI). However, the output range comprises of the value 15-45 for insulin dose.

Table 2.3 Ranges of the input and output variables

Input		Output
AFBGL	**ADPI**	**Insulin Dose**
6-19	30-100	15-45

Table 2.4 also illustrates the fuzzy value breakdown into L (Low), O (Optimum) and H (High) for both AFBGL and ADPI. It also includes a particular range and the unity membership point for each fuzzy value breakdown. In the unity membership point, the value of membership function becomes one.

Table 2.4 Ranges and unity membership points of input variables (AFBGL and ADPI)

AFBGL			ADPI	
Fuzzy Values	**Ranges**	**Unity Membership Points**	**Ranges**	**Unity Membership Points**
L	6-12.5	9.25	30-65	47.5
O	9-15.5	12.5	45-85	65
H	12.5-19	15.75	65-100	82.5

From table 2.4 it is observed that there are different unity membership points for each range of the fuzzy values. The 'unity membership point' symbolizes the point where the membership function earns a membership valuation of one. It means an AFBGL of 9.25 signifies an absolute low average fasting blood glucose level. Similarly, an ADPI of 82.5 suggests a perfectly high average daily protein intake. It is to mention that, any other values of ADPI in 65-100 is also suggestive for fuzzy value high (H), but with a lower degree of membership. In this case, the membership value is less than one. Table 2.5 shows the ranges and unity membership points of output variable (Insulin Dose). The unity membership points 20 on Table 2.5 for insulin dose suggests that it falls ideally on fuzzy value A. On this table, five fuzzy values with different ranges have five particular unity membership points.

Table 2.5 Ranges and unity membership points of output variables (Insulin Dose)

Insulin Dose		
Fuzzy Values	**Ranges**	**Unity Membership Points**
A	15-25	20
B	20-30	25
C	25-35	30
D	30-40	35
E	35-45	40

Similarly, the unity membership point 25 on Table 2.5 for insulin dose proposes that it falls correctly on fuzzy value B. The unity membership points 30, 35 and 40 on the table too recommend that these values fall flawlessly on fuzzy value C, D and E respectively.

Membership functions (MFs) are said to be the elementary units of fuzzy set theory. The fuzziness of the fuzzy logic technique is best outlined by the membership function. There are several types of membership functions to describe a fuzzy set (Mahfouf et al., 2001). Such as-

1. Triangular
2. z-shape
3. Trapezoidal
4. s-shape
5. Sigmoid and
6. Gaussian

There are different number of parameters for different membership functions. Triangular membership functions are described by three parameters, such as – a,b and c. There are four parameters for expressing trapezoidal membership functions. These parameters are – a, b, c and d. the two parameters required to express Gaussian membership functions are - c and σ. Here, c is the membership functions centre and by using σ we can determine the width of the membership function. A sigmoid membership function is defined by the parameter 'a'. Here, the controller of the slop is 'a'.

There are different features of the membership function. These features are – core, support and boundary. Core is the area of the fuzzy set that is indicated by a complete membership in the fuzzy set. Support and boundaries are the areas those are indicated by a non-zero and a non-zero but insufficient enrollment in the set respectively (Sproule, Naronjo, & Turksen, 2002).

In this study, the MATLAB Fuzzy Logic Toolbox is used for constructing all the triangular membership functions (L, O and H) of the input variables average fasting blood glucose level (AFBGL) and average daily protein intake (ADPI). Figure 2.1A shows the membership functions for AFBGL_L constructed in accordance with the ranges and unity membership points defined in Table 2.4.

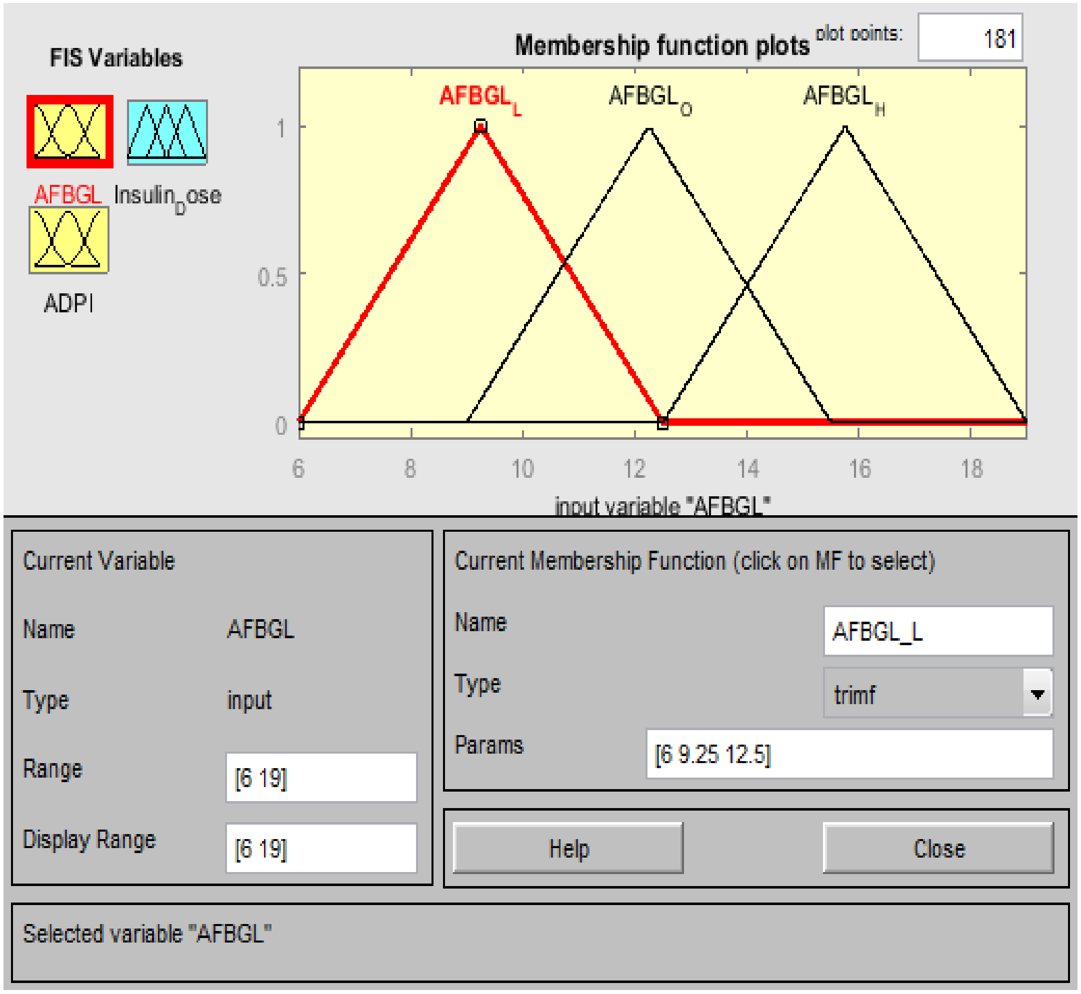

Figure 2.1A Membership function for AFBGL_L

In this figure, the variable selected was average fasting blood glucose level (AFBGL) having a range of 6-19. The parameters set for plotting this membership function was 6, 9.25 and 12.5. The presented figure depicts the overlapping between AFBGL_L, AFBGL_O and AFBGL_H.

The membership functions for AFBGL_O and AFBGL_H, those were also constructed in accordance with the ranges and unity membership points defined in Table 2.3 are shown in figure 2.1B and 2.1C respectively. The parameters set for plotting the membership function for AFBGL_O were 9, 12.25 and 15.5, whereas the parameters set for plotting the membership function for AFBGL_H were 12.5, 15.75 and 19. These two figures have portrayed the overlapping between AFBGL_L, AFBGL_O and AFBGL_H.

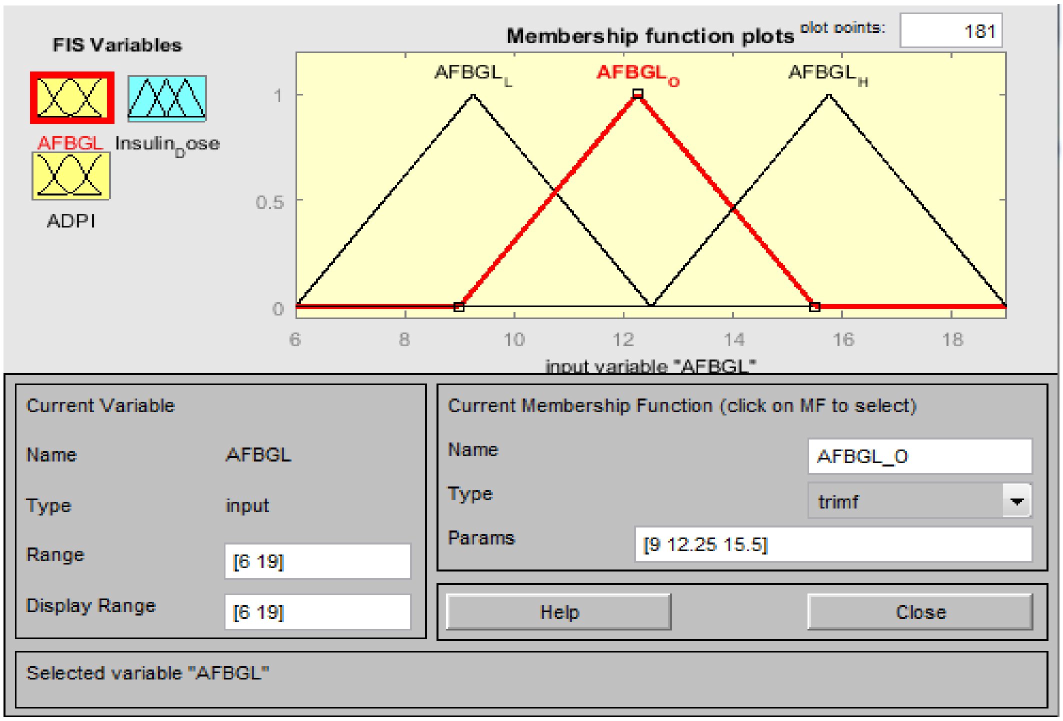

Figure 2.1B Membership function for AFBGL_O

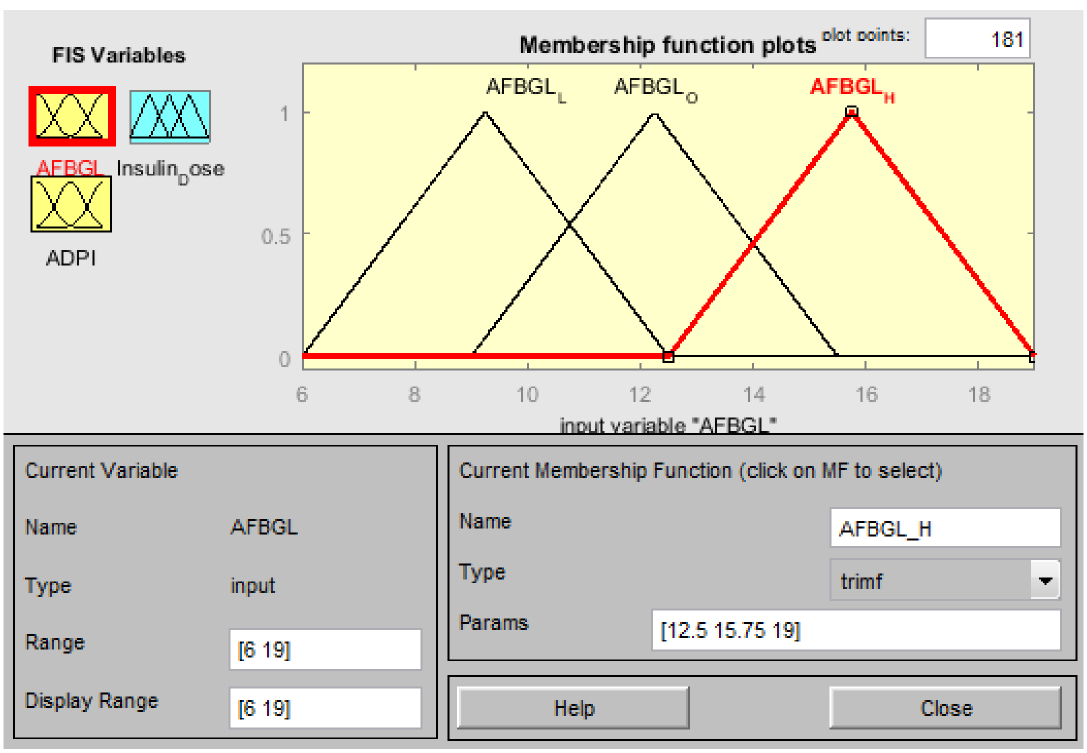

Figure 2.1C Membership function for AFBGL_H

The second input variable ADPI too has membership functions of L, O and H. For this variable the ranges and unity membership points to construct membership function is taken from Table 2.4. Below, Figure 2.1D illustrates the triangular membership functions constructed for ADPI_L.

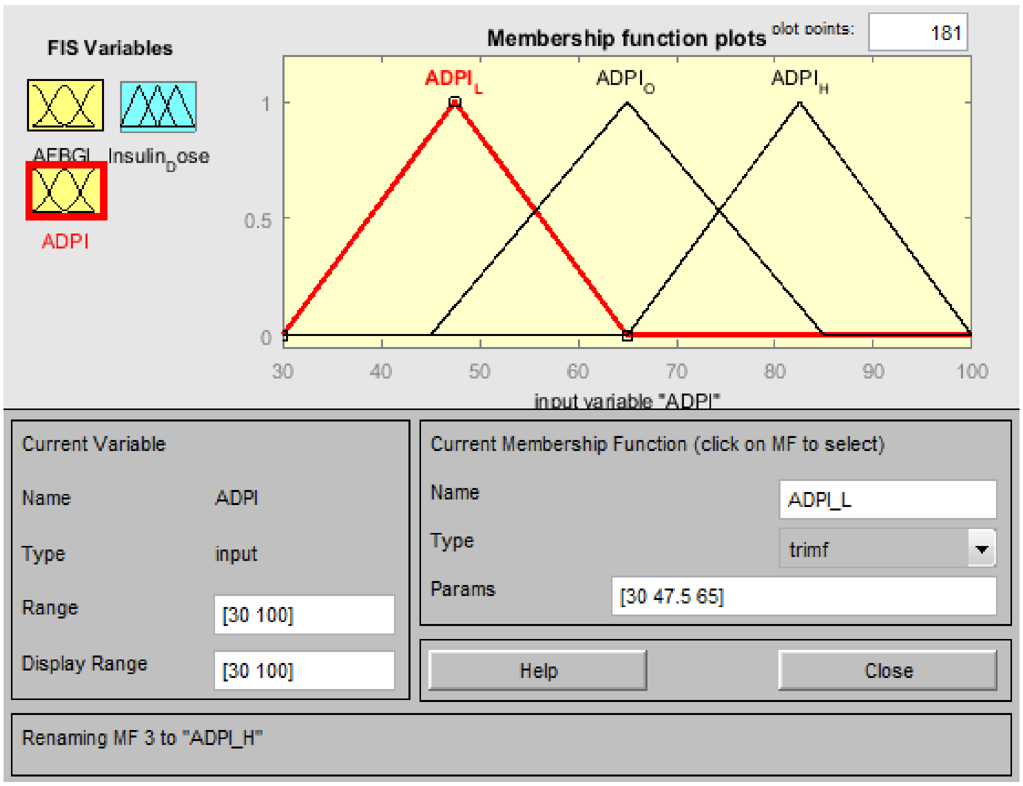

Figure 2.1D Membership function for ADPI_L

In the figure presented above, the variable selected was average daily protein intake (ADPI) with the lowest value of 30 and the highest value of 100. The parameters set for plotting this membership function were 30, 47.5 and 65. The presented figure also depicts the overlapping between ADPI_L, ADPI_O and ADPI_H.

Figure 2.1E and Figure 2.1F have shown below the triangular membership functions constructed for ADPI_O and ADPI_H respectively. The parameters set for plotting the triangular membership function of ADPI_O were 45,65 and 85. Similarly, the parameters set for plotting the triangular membership function of ADPI_H were 65, 82.5 and 100.

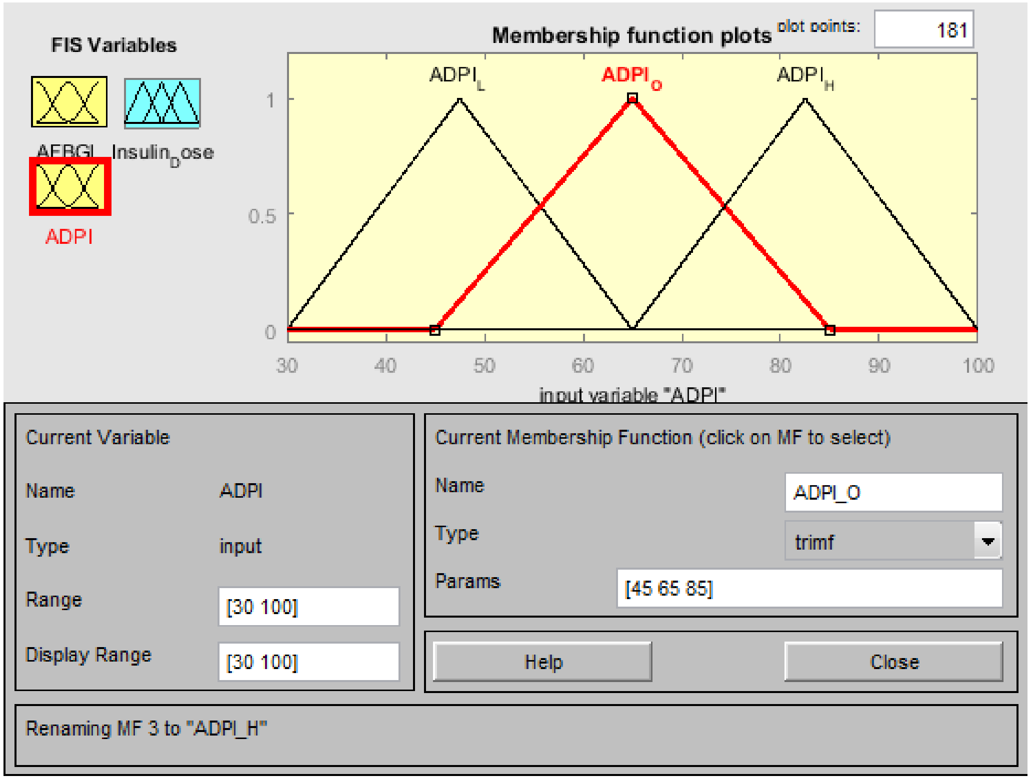

Figure 2.1E Membership function for ADPI_O

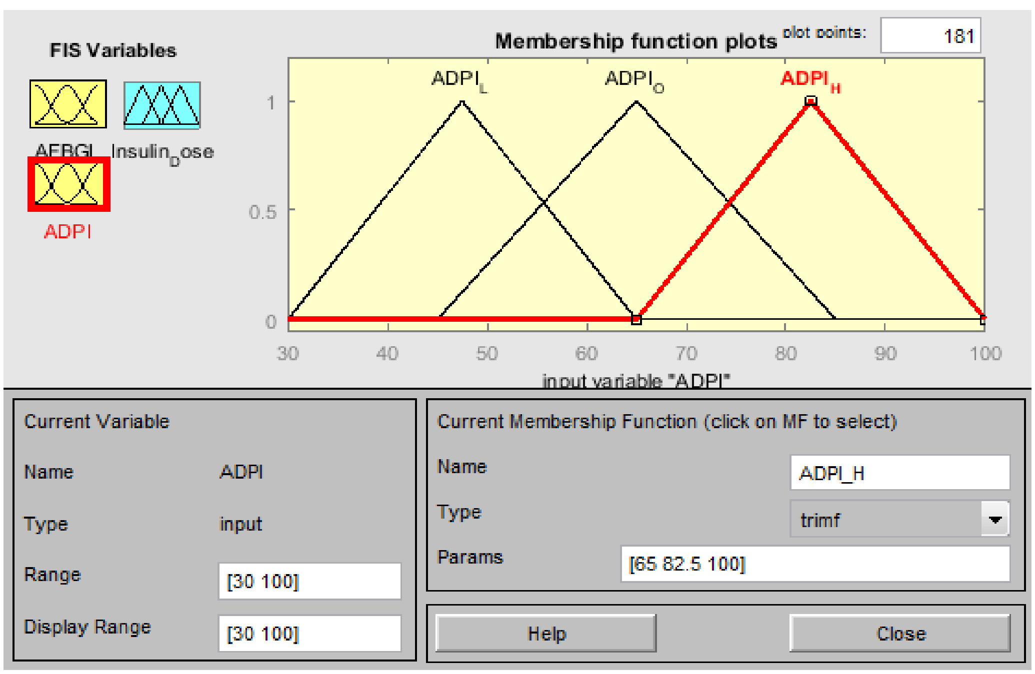

Figure 2.1F Membership function for ADPI_H

The final set of triangular membership function consisting of five membership functions (A, B, C, D and E) is that of the output variable (Insulin Dose). Figure 2.1G, 2.1H, 2.1I, 2.1J and 2.1K express the membership function for different fuzzy values of insulin dose.

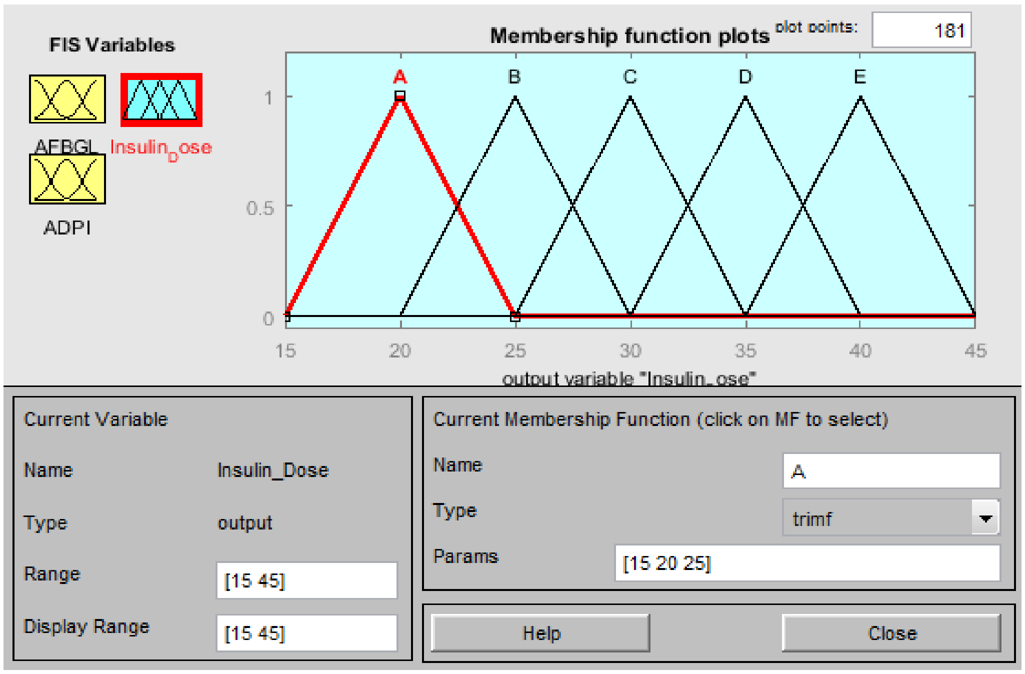

Figure 2.1G Membership function for Insulin_Dose_A

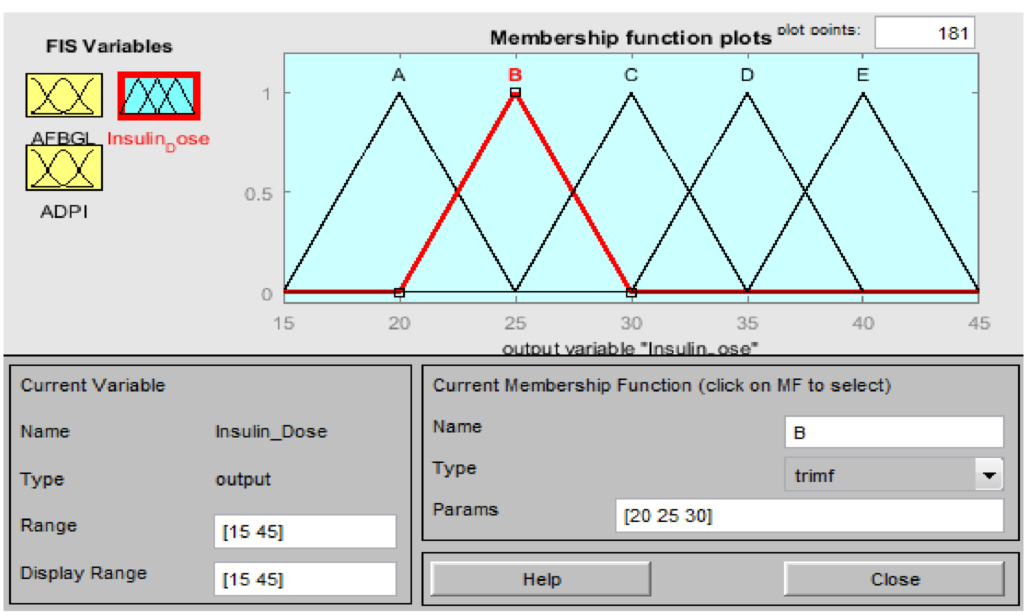

Figure 2.1H Membership function for Insulin_Dose_B

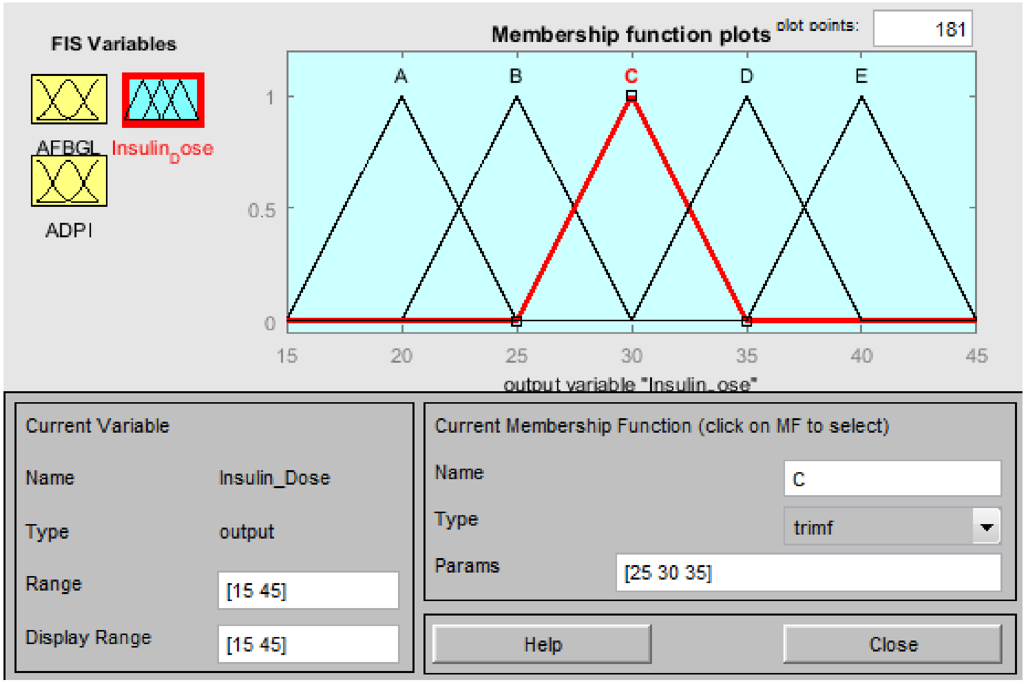

Figure 2.1I Membership function for Insulin_Dose_C

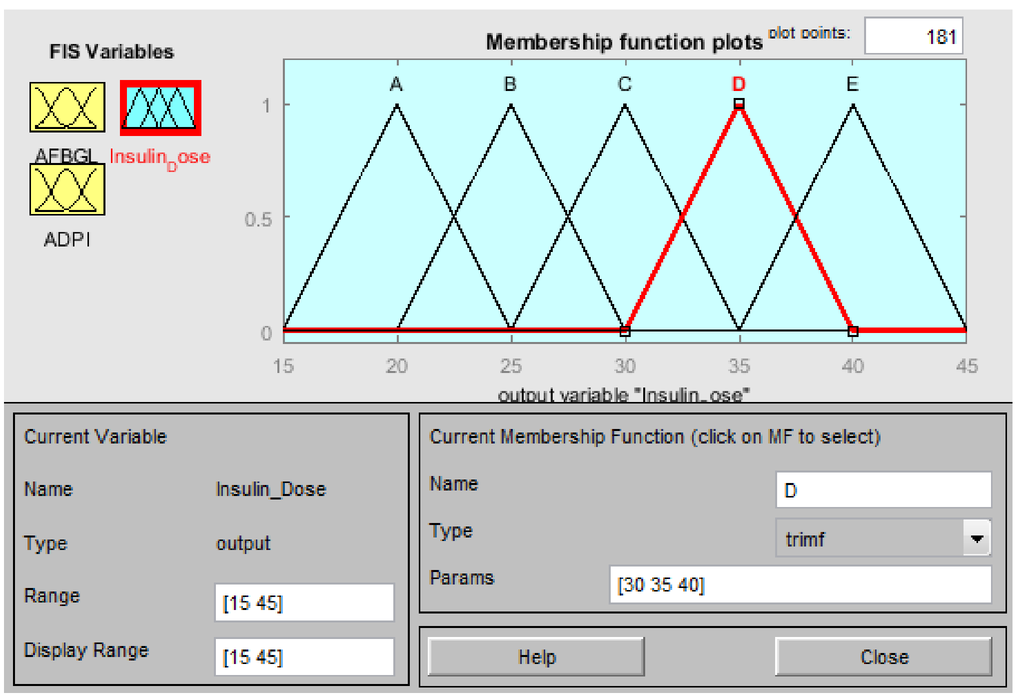

Figure 2.1J Membership function for Insulin_Dose_D

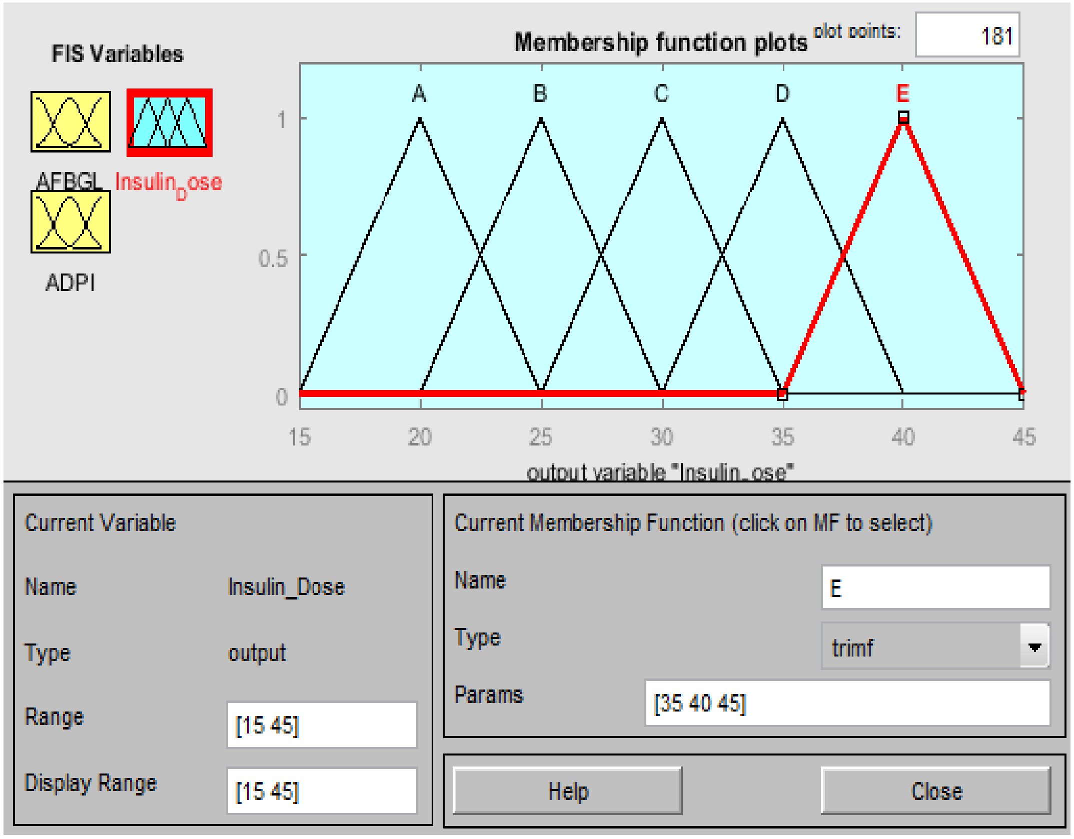

Figure 2.1K Membership function for Insulin_Dose_E

To summarize the fuzzification of membership functions, this system is a two inputs-one output system. Each input and output have different fuzzy values, ranges and unity membership points, which have described in Table 2.3, 2.4 and 2.5. Every membership function constructed here is triangular with varying overlapping regions that are displayed through Figure 2.1A to Figure 2.1K.

2.3.2 Rules for fuzzy inference definition

Rules are set to support the fuzzy system with a decision-making capacity. In the previous section, the membership functions were defined, but no relationship was established among these membership functions so far. This section deals with setting rules for the inference in order to build up an input/output relation so that the system can work in accordance. For setting the rules, the if/then connections are used. The Table 2.6 given below shows the decision matrix where if/then rules are set.

Table 2.6 The decision matrix

Decision Matrix			
AFBGL/ADPI	**L**	**O**	**H**
L	C	C	D
O	D	C	D
H	D	D	E

From the Table 2.6, it is seen that, if the patient has low AFBGL (6-12.5) an optimum ADPI (45-85), then for that patient the output as insulin dose is C (25-35). Likewise, the patient with a high AFBGL (12.5-19) and low ADPI (30-65), needs to administer an insulin dose that falls in the range D (30-40). These phenomena are stated in the system as ‘if (AFBGL is AFBGL_H) and (PI is PI_L) then (Inulin_Dose is D)’. The entire if/then rules are fixed in accordance with the decision matrix which is given below:

1. If (AFBGL is AFBGL_L) and (PI is PI_L) then (Inulin_Dose is C)

2. If (AFBGL is AFBGL_O) and (PI is PI_L) then (Inulin_Dose is D)

3. If (AFBGL is AFBGL_H) and (PI is PI_L) then (Inulin_Dose is D)

4. If (AFBGL is AFBGL_L) and (PI is PI_O) then (Inulin_Dose is C)

5. If (AFBGL is AFBGL_O) and (PI is PI_O) then (Inulin_Dose is C)

6. If (AFBGL is AFBGL_H) and (PI is PI_O) then (Inulin_Dose is D)

7. If (AFBGL is AFBGL_L) and (PI is PI_H) then (Inulin_Dose is D)

8. If (AFBGL is AFBGL_O) and (PI is PI_H) then (Inulin_Dose is D)

9. If (AFBGL is AFBGL_H) and (PI is PI_H) then (Inulin_Dose is E)

So far, the fuzzy rules suggest a range of Insulin Dose for the patients. To refine it further, defuzzification (discussed in section 2.3.3) is done. After defuzzification, a definite point of insulin dose as output is obtained.

2.3.3 Defuzzification for the fuzzy inference

The final step of the fuzzy inferencing is called defuzzification. It is done to polish the insulin dose range; got after carrying if/then rules in the system. After defuzzification, a precise value of insulin dose is recommended as the output. In this study, the default method of fuzzification 'centroid' is used that offers the finest closeness. Figure 2.2A depicts the defuzzification process for a set of inputs of patient 1 carried out in the rule viewer feature of MATLAB Fuzzy Logic Toolbox and advice a precise number for insulin dosage as an output.

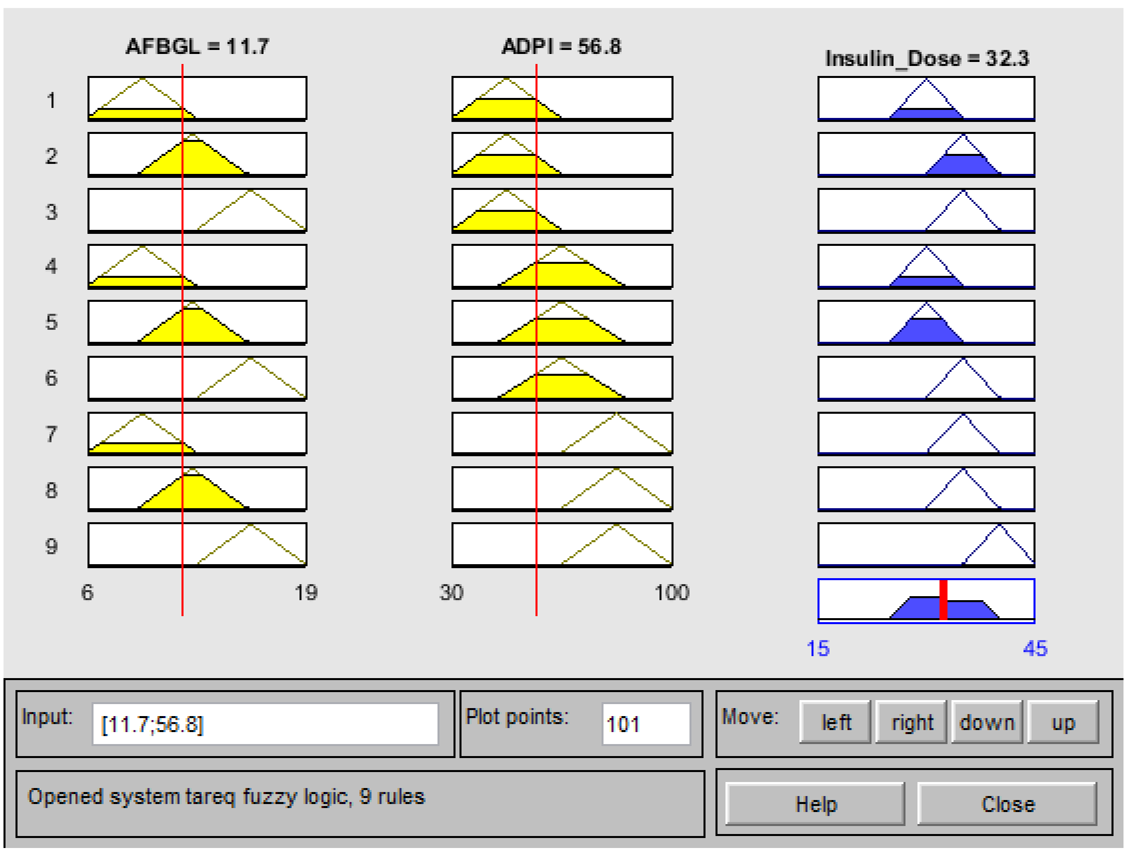

Figure 2.2A A recommendation of insulin dosage for patient 1 returned by the fuzzy logic system

In Figure 2.2A, it is noticed that, for a subject of AFBGL=11.7 mmol/L and ADPI=56.8 gm, the recommended insulin dosage returned by the fuzzy system for that subject is 32.3 units.

The following figures outline the recommended insulin dosage returned by the fuzzy system for the other patients:

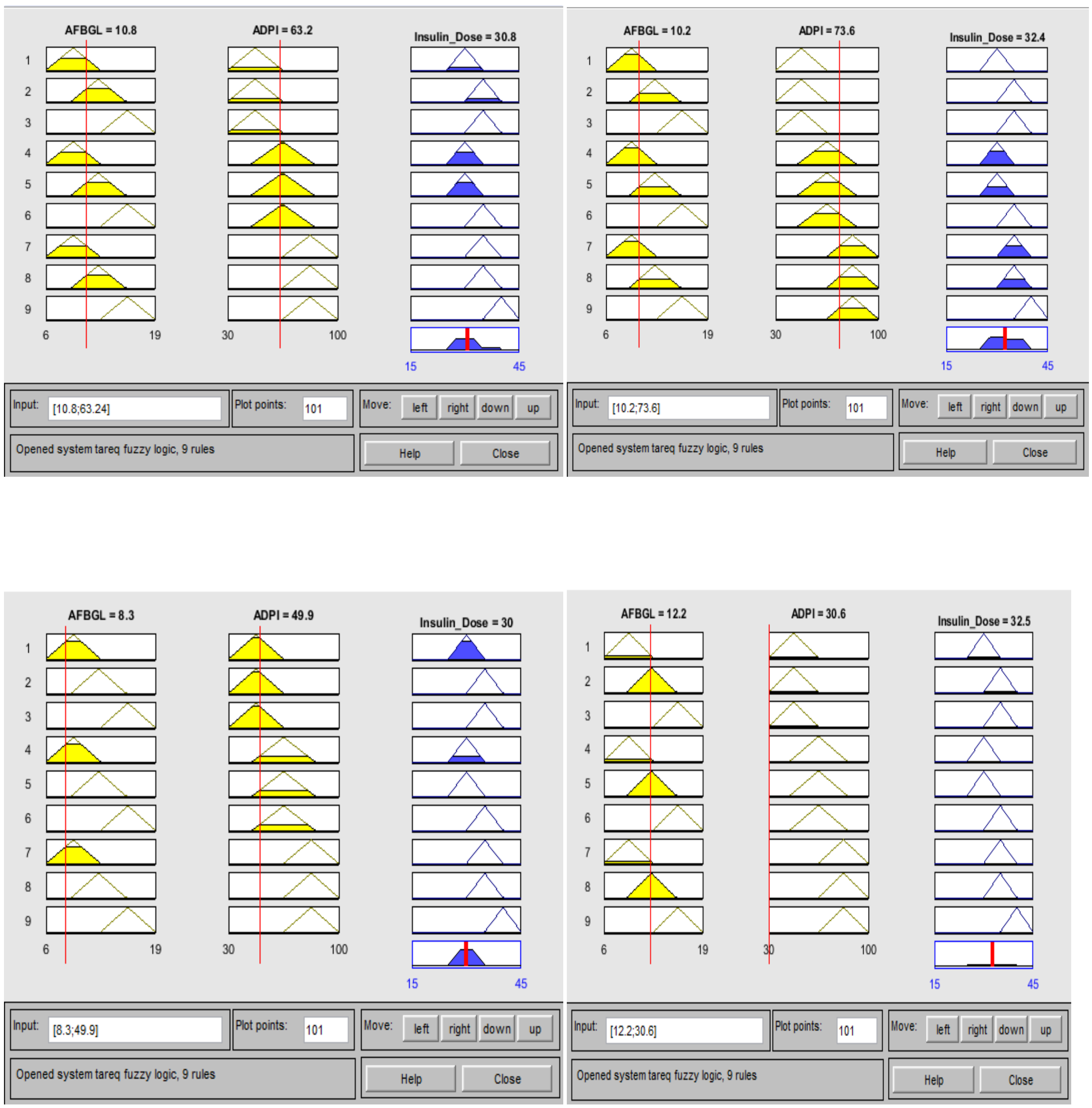

Figure 2.2B A recommendation of insulin dosage for patients 2, 3, 4 and 5 returned by the fuzzy logic system starting from up to down (left to right)

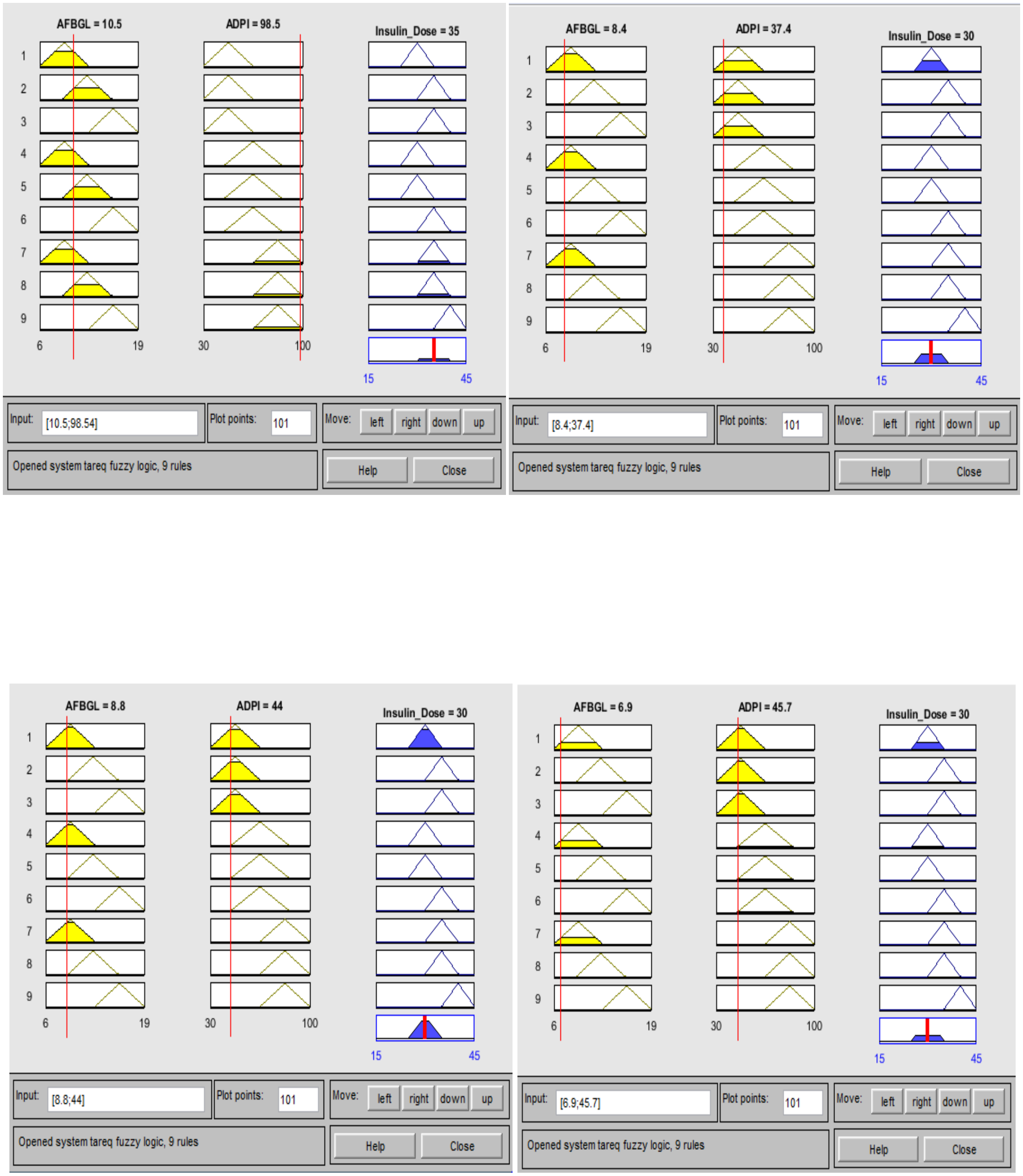

Figure 2.2C A recommendation of insulin dosage for patients 6, 7, 8 and 9 returned by the fuzzy logic system starting from up to down (left to right)

Figure 2.2D A recommendation of insulin dosage for patients 10, 11, 12 and 13 returned by the fuzzy logic system starting from up to down (left to right)

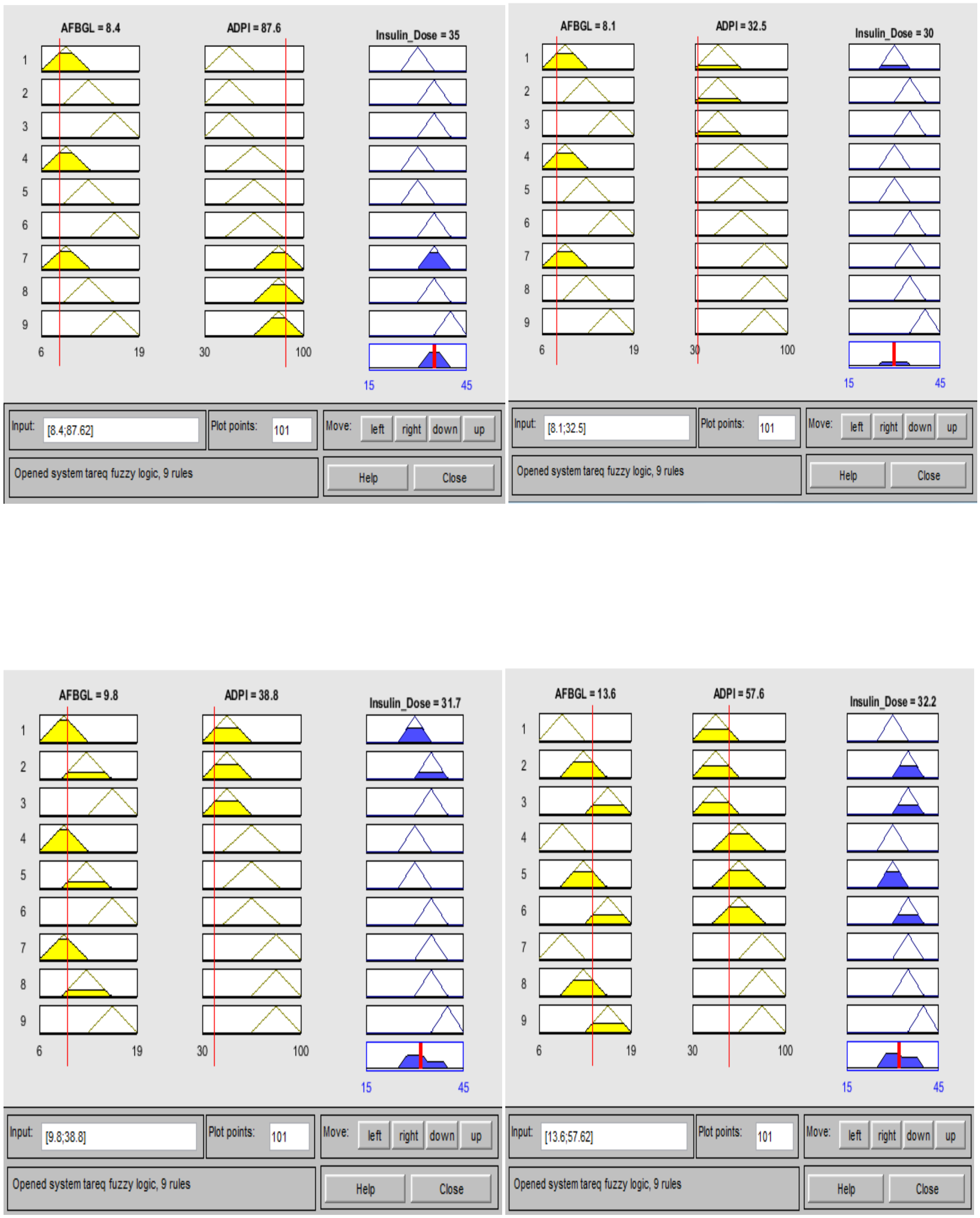

Figure 2.2E A recommendation of insulin dosage for patients 14, 15, 16 and 17 returned by the fuzzy logic system starting from up to down (left to right)

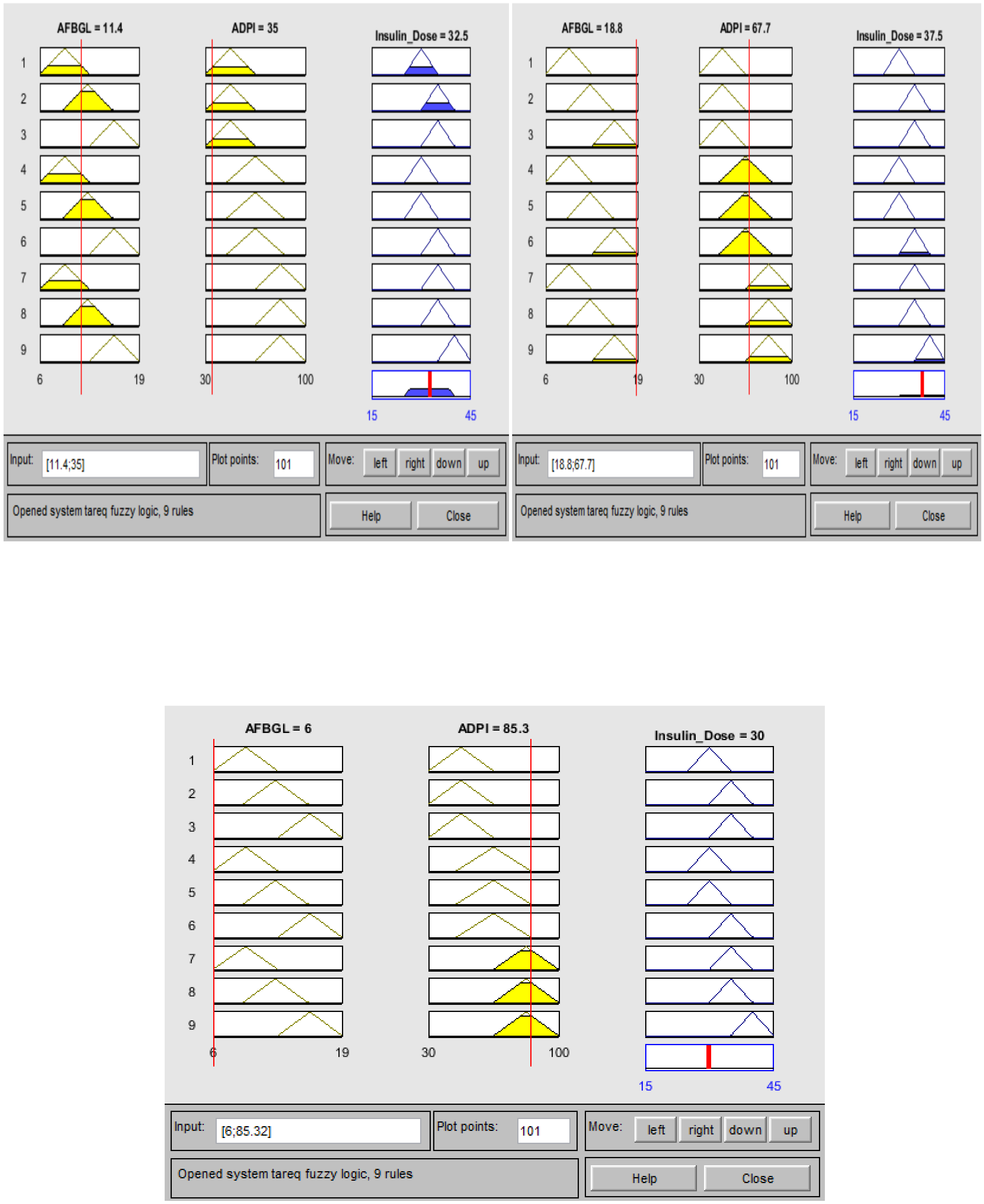

Figure 2.2F A recommendation of insulin dosage for patients 18, 19 and 20 returned by the fuzzy logic system starting from up to down (left to right)

2.3.4 Surface diagram for the fuzzy inference

The surface diagram is a component of the MATLAB Fuzzy Logic Toolbox that enlightens us by providing a visual illustration of the whole system through a three-dimensional surface. It shows the relationship among input variables and output variable at a time. Figure 2.3A and Figure 2.3B display the three-dimensional relationships among input variables (AFBGL and ADPI) and output variable (Insulin Dose).

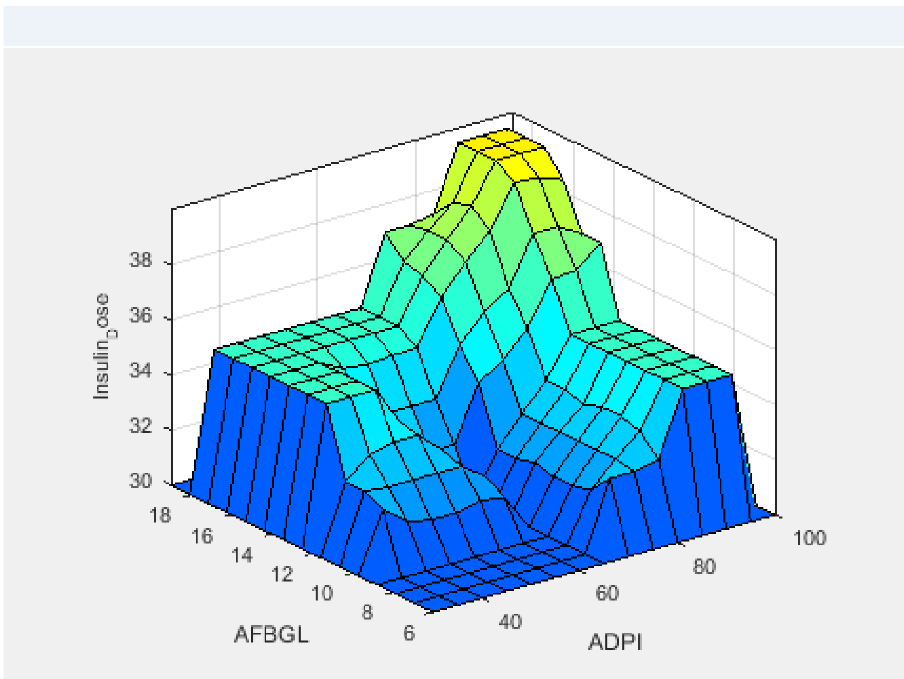

Figure 2.3A Surface diagram of Insulin Dose against AFBGL (X-axis) and ADPI (Y-axis)

In Figure 2.3A input variable AFBGL is selected as X-axis and another input variable ADPI is selected as Y-axis. The output variable Insulin Dose was fixed as Z-axis. After plotting these data, the outcome is a three-dimensional (3-D) surface diagram, visually representing the relationship among these variables.

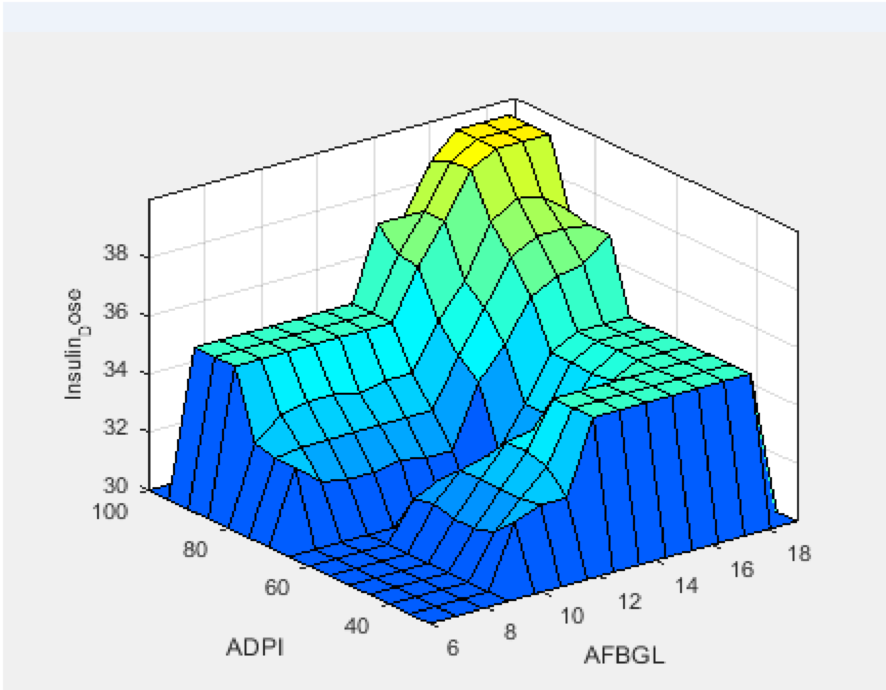

Figure 2.3B Surface diagram of Insulin Dose against ADPI (X-axis) and AFBGL (Y-axis)

Likewise, the previous Figure here input variable ADPI was chosen as X-axis and AFBGL as Y-axis. The output variable Insulin Dose has remained as Z-axis. The surface viewer of Fuzzy Logic Toolbox returned the 3-D surface diagram of Figure 2.3B.

Chapter 3

Results and Discussions

3.1. Results

The 20 patients considered in this research were all admitted to BSMMU and BIRDEM with a known history of T2DM. These patients had other complications that were reported during the interview. All of these patients' treatment procedure includes insulin therapy on a regular basis adjusted by the respective physician of the ward to treat their diseases. These physicians' prescribed insulin doses were then compared to the predicted insulin doses by the fuzzy system. Table 3.1 elaborates the comparison between physicians' prescribed insulin dose and predicted insulin dose by the fuzzy system for each patient.

Table 3.1 Predicted dose Vs Prescribed dose of daily insulin units for each of the 20 patients

Patient No	Predicted insulin dose by the fuzzy system (PID)	Physicians prescribed insulin dose (PPD)	Numerical difference
1	32.3	32	0.3
2	30.8	26	4.8
3	32.4	34	-1.6
4	30	17	13
5	32.5	34	-1.5
6	35	34	1
7	30	25	5
8	30	22	8
9	30	33	-3
10	35	39	-4
11	35	30	5
12	30	29	1
13	35	20	15
14	35	31	4
15	30	32	-2
16	31.7	34	-2.3
17	32.2	30	2.2

18	32.5	44	-11.5
19	37.5	42	-4.5
20	30	22	8

There observed numerical differences of varying degrees between the predicted insulin dose (PID) and the physicians' prescribed insulin dose (PPD) suggested by the fuzzy logic based computational system. The cases where predicted insulin dose by the fuzzy system is greater than that of physicians prescribed insulin dose, the numerical difference calculated is seen as positive. Whereas, the situations where PID is lower than that of PPD, the numerical difference computed is negative. No case has seen where predicted dose and prescribed dose are the same.

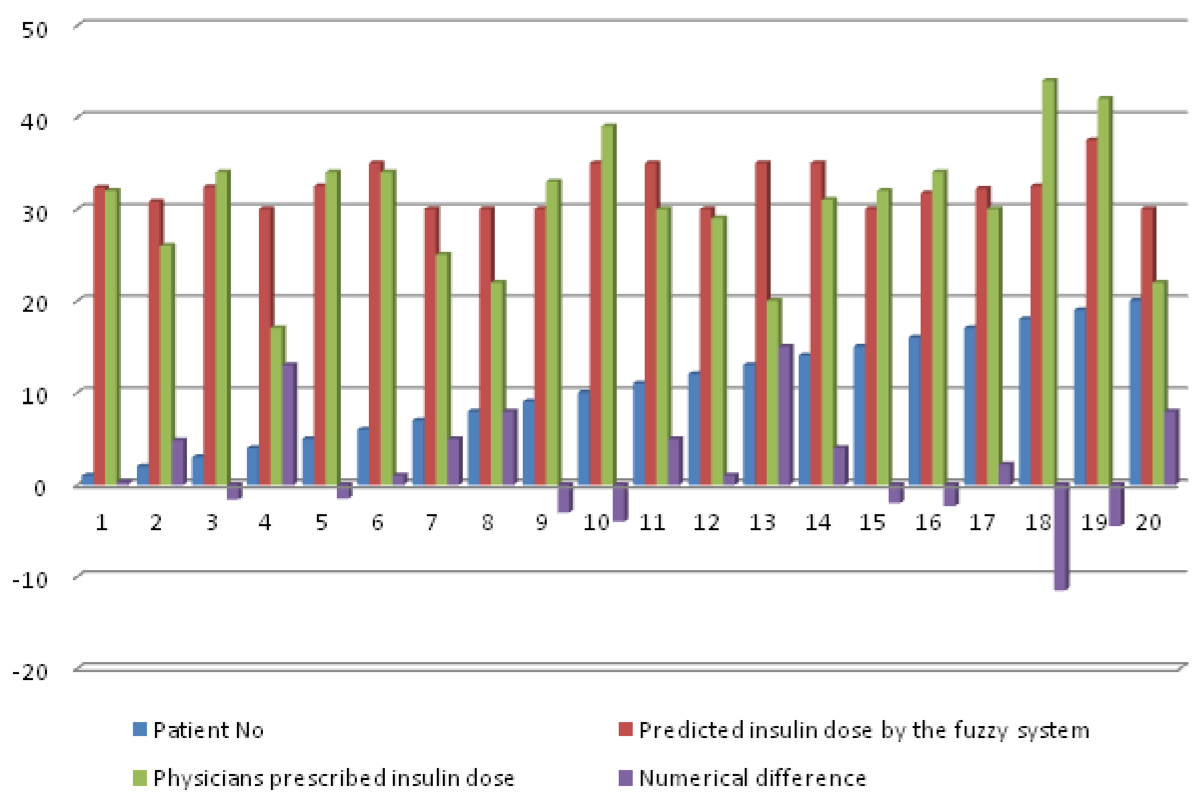

Figure 3.1 3-D Clustered Column comparing the values of predicted insulin dose & prescribed insulin dose for each patient

The figure 3.1 graphically compares the values of predicted insulin dose (PID) and physicians prescribed insulin dose (PPD) with their numerical differences against each of the 20 patients. It exerts a visual idea of how much the values of PID and PPD differs for each patient.

3.2. Discussion

The core objective of this study was to refine the insulin dose of T2DM patients prescribed by physicians in order to reduce the hyperglycemic and hypoglycemic events in the future. The predicted insulin dose by the fuzzy system scrutinizes the physicians prescribed insulin dose with the help of numerical differences. The positive numerical difference indicates the patient is administering less unit of insulin comparing to the predicted dose. Thus, the patient incurs the risk of experiencing hyperglycemic events, other words increasing the chances of mortal complications associated with T2DM. Similarly, a negative numerical difference suggests the administration of more insulin dose by the patients. Therefore, a possibility of hypoglycemic events is probable. This means the patient requires fewer units of insulin dose to treat the disease. However, the patient is administering insulin in higher amounts and in a pathway of costing more money to supply the higher units of insulin. It thus is creating a physiological crisis for the future of the patient and harming financially.

Table 3.2, in brief, exhibits the interpretation of input-output values for each patient. The aim of this table is to discuss the significance of fuzzy based output regarding the treatment of each patient in achieving a good quality of life. For this, in the table, suggestive condition for each patient was identified based on the numerical differences between PPD and PID. These suggestive conditions were justified by comparing them with the evident conditions documented during the interview period for each patient. The comparison between the suggestive condition and evident condition thus provides us with an intact overview of the whole study.

To review distinctly, patient 2 had an average fasting blood glucose level (AFBGL) of 10.8 mmol/L and average daily protein intake (ADPI) was 63.24 gm. The prescribed insulin dose (PPD) of this patient by the physician was 26. However the fuzzy-based system has predicted (PID) an insulin dose of 30.8 units for this patient. The numerical difference between PPD and PID for this patient is +4.8. Thus, it is suggestive that the patient is in the danger of suffering from high blood sugar (HBS) or hyperglycemic episodes in the future.

Table 3.2 Interpretation of input-output values for some patients

Pt No.	Reported HBS/LBS events during interview week, FASTING	Reported HBS/LBS events during interview week, ABF	Reported HBS/LBS events during interview week, AL	Reported HBS/LBS events during interview week, AD	Numerical difference by fuzzy system	Suggestive HBS event/ LBS event	Evidence of HBS event/ LBS event
2	11.3, 8.9, 12.1	13.4, 17.6	17.9,	17.1, 14.2	4.8	HBS	HBS
7	7.3, 7.6, 6.7, 11.9	14.1, 21.9	12.3, 21.6	19.1, 21.9	5	HBS	HBS
16	--	3.2	3.8	--	-2.3	LBS	LBS
20	--	--	12.3,	11.9	8	HBS	HBS

In the documentation of this patient, it is evident that he had experienced hyperglycemic events for a number of times during the week of this interview. He had encountered with the blood glucose level of 17.6 mmol/L after breakfast, 17.9 mmol/L after the meal and once reported 12.1 mmol/L fasting blood glucose. It thus demonstrates the implication and significance of the polished insulin dosing by the fuzzy logic based system. The administration as per predicted insulin dose may enlighten this patient with less chance of having hyperglycemic events in future. Also, there has drawn a numerical difference of -2.3 for the patient 16. Though the PPD reported for this patient was 32, the PID received through the fuzzy system is 30. As per the hypothesis, the patient is in a jeopardy of encountering with low blood sugar (LBS) or hypoglycemic event hereafter. Certainly, the evidence compiled against this patient reveals that she had suffered from hypoglycemic events twice during the interview period. She was identified with a blood glucose of 3.2 mmol/L after having breakfast and 3.1 after lunch. Moreover, the patient costing more to administer the higher units of insulin which retard her economic finance. Thus, governing the predicted insulin dose may reduce her hypoglycemic events and higher her economic output in the long run. The case of patient 20 testifies to an AFBGL of 6 mmol/L while having a high ADPI value of 85.32 gm by the patient. The PPD for this patient was documented as 22 units. However, the refined insulin dose predicted by the system (PID) for this case is 30. The numerical difference, in this case, is +8. Though the patient has reported two hyperglycemic events during the interview period after the meal rather than this, he had a good control over his blood glucose level. Concisely, it can be inferred that the insulin dose that fuzzy logic has provided in this patient considering the two patient-reported factors i.e. the average fasting blood glucose level (AFBGL) and average daily protein intake (ADPI) may support the urge of promising a better quality of life through ensuring better precision over probable estimation. The output analysis of patient 7 demonstrates that the numerical difference between PPD and PID for this patient is +5 suggestive for hyperglycemic events. There are evidences of several hyperglycemic events suffered by this patient documented as a blood glucose level of 11.9 mmol/L (fasting), 14.1 mmol/L, 15.9 mmol/L, 21.6 mmol/L, 19.1 mmol/L, 21.9 mmol/L and 12.3 mmol/L; all claimed to recorded after meal.

Far from the lucid outcomes for most patients, there observed some PIDs where the patient did not reasonably be favored by this fuzzy logic based system, notably in the cases for the patient 10, patient 12 and patient 18. We hypothesized that other factors involved in the patient’s lifestyle and physiology might have harmed its accuracy. To point out, in the case of patient 10, there reported a high protein intake in the patients' physiology along with some other complex diseases. These dietary exceptions and the interaction of different drugs might be the reason for his defective output. Furthermore, patient 12 reported the lowest AFBGL and a longer duration of diabetes. These could be the cause for this patient not to get a positive outcome from the fuzzy logic based system. Furthermore, patient 18 was a recently diagnosed diabetes patients and there were insufficient data of his dietary protein intake which we believe to be the reason for the faulty outcome from this system.

Chapter 4

Conclusion & Future Scope

4.1 Conclusion

The people affected by type 2 diabetes is increasing day by day for which the faulty administration of insulin is a matter of concern that may be caused by prescribing insulin dose by considering less patient-reported factors (PRFs). Hence, a concurrent review of more patient-reported factors is vital to recommend a more precise, accurate and personalized insulin dose for these patients where artificial intelligence comes in. The study has shown a numerical difference of varying degrees between the physicians prescribed insulin dose (PPD) and predicted insulin dose (PID) for every patient. The positive difference that hypothesized that the patient is in danger of facing hyperglycemia has met supportive evidence of previous hyperglycemic events experienced by the patient. Similarly, a negative numerical difference is also supported by the reported hypoglycemic events. We can see that the research has demonstrated an improved glucose regulation for the patients affected by T2DM by the fuzzy logic based system. The occurrences of patient no. 2, 7, 16 and 20 have seemingly stated the pitfalls of the traditional insulin dosing system based on what their treatment procedure was going on and the significance of prescribing insulin dose by the fuzzy logic based system. This technique is able to establish a more meaningful and definite insulin dosing for these patients that may help them to lead a healthier life as well as benefit them with finances. However, the quality of output generated by artificial intelligence (AI) technology absolutely depends on the quality of input data. Accordingly, this study has recorded a number of anomalies and miscalculation for a number of patients that required to be refined by adding more PRFs those exerting effects on their blood glucose level. The more PRFs are taken into simultaneous consideration the further refined the output. Thus, further study of this kind with more number of patients with their PRFs are suggested for improving the health outcome.

4.2 Future scope

Like other areas, Artificial Intelligence (AI) technology has now widely been used in the health care sector worldwide for its potential to provide more accuracy in any complex analysis of data related to health. A recent award winning prototype 'Cardioexplorer' has used artificial intelligence based modeling process MPA (Memetic pattern-based algorithm) and demonstrated to help health-care professionals including doctors in the diagnosis and decision-making mechanism of suspected cardiovascular patients without any invasive procedure (Zellweger et al., 2018). Next, a new study on the application of ML (Machine Learning) that is a form of artificial intelligence summarized the significance of artificial intelligence technology in the field of diagnosis and imaging. This research showcased the advantages of the computational system over traditional procedure such as– time-saving, manpower cost and accuracy (Nichols, Herbert Chan, & Baker, 2018). Furthermore, the fuzzy logic-based system has experimented in many divergent and vital areas of health sciences. Especially, this system has been used in the mechanical control of drug delivery devices i.e. intensive care setting & surgical units and diagnosis of disease. Fuzzy logic is applied in controlling arterial pressure with isoflurane, enflurane anesthesia, controlling hypertension during anesthesia and also in the case of neuromuscular blocker (Sproule, Naronjo, & Turksen, 2002). Nowadays, the computational tool to integrate data is one of the most interesting topics to investigate among medical researchers for achieving more accuracy in disease diagnosis (Ahmadi et al., 2018). The schematic review done by a group of researchers pointed out the advantages of the computer-aided fuzzy logic based method in the diagnosis of some chronic & acute disorders like- fever, heart failure, lung cancers, diabetes mellitus, electronic disorders with tremendous precision (Ahmadi et al., 2018). Personalized medicine is crucial in patients with numerous disease conditions to serve them a risk-free treatment. Machine learning can be an evolutionary support for the physicians in bringing this personalized medicine system to recommended patients (Fröhlich et al., 2018). In addition to the diagnosis of chronic and acute disorders, fuzzy logic is presently using as a reliable tool in the molecular level classification of breast cancer that allows a better prediction outcome for breast cancer patients. (Kempowsky-Hamon et al., 2015). Further expansion of this type of research is advised on the drugs that have a narrow therapeutic index and where the environmental or clinical factors influence the outcome of the drugs. It needs to restate that the artificial intelligence (AI) can never be considered as the replacement to a physician. Rather, AI-based systems are thought-out to be the constructive tools to support physicians in their decision-making steps, provide more accuracy and utilize the resources of feasible biomedical expertise.

Chapter 5

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