



## Retrospective Investigation of Complication Development Risk Conditions with Logistic Regression Models in Diabetic Patients

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### Abstract

Diabetes is one of the most important diseases that threaten human health in recent years. The diagnosis of diabetes can be made as a result of many medical examination findings, analyzes and examinations. The development of complications in patients evaluated with this diagnosis carries very serious risks for the patient. The accurate and reliable prediction of risk situations will contribute positively to the decision making process of physicians. The data obtained with the help of the developments in information technologies can be processed much faster and reliably. The logistic regression analysis was chosen among the available methods to analyze the data in terms of being the suitable for simplicity and accuracy targets. As a result of the logistic regression analysis; age, HbA1C and some lipid parameters have an effect on complication development. In addition, diabetes complication types were determined specifically and the effects of the factors causing complications were investigated.

*Keywords: Diabetes, Logistic Regression Analyses, HbA1C, Peripheral Circulatory Complication.*

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## Diyabetik Hastalarda Komplikasyon Geliştirme Riski Durumlarının Lojistik Regresyon Modelleri ile Retrospektif İncelenmesi

### Özet

Son yıllarda insan sağlığını tehdit eden en önemli hastalıklardan birisi diyabettir. Diyabet tanısı birçok tıbbi muayene bulgusu, tetkik ve tetkikler sonucunda konulabilmektedir. Bu tanı ile değerlendirilen hastalarda komplikasyon gelişmesi hasta için çok ciddi riskler taşımaktadır. Risk durumlarının doğru ve güvenilir bir şekilde öngörülmesi hekimlerin karar verme süreçlerine olumlu katkı sağlayacaktır. Bilgi teknolojilerindeki gelişmeler sayesinde elde edilen veriler çok daha hızlı ve güvenilir bir şekilde işlenebilmektedir. Lojistik regresyon analizi, basitlik ve doğruluk hedeflerine uygun olması açısından verileri analiz etmek için mevcut yöntemler arasından seçilmiştir. Lojistik regresyon analizi sonucunda; yaş, HbA1C ve bazı lipid parametreleri komplikasyon gelişiminde etkilidir. Ayrıca diyabet komplikasyon tipleri spesifik olarak belirlenmiş ve komplikasyonlara neden olan faktörlerin etkileri araştırılmıştır.

*Anahtar sözcükler: Diyabet, Lojistik Regresyon Analizi, HbA1C, Periferik Dolaşım Komplikasyonu.*

### 1. Introduction

Diabetes, which has become widespread in the world in recent years due to improper diet and sedentary lifestyle, is estimated to cause four million deaths in 2019, according to the International Diabetes Federation (IDF). One of eleven adults (about 463 million people) between the ages of 20-79 in the world is diabetic. One of the two adults (232 million) with this disease has not yet been diagnosed. One in five people with diabetes is over 65 years old. 10% of global health spending (\$ 760 billion) is spent on diabetes. Three out of every four people with diabetes (79%) have been lived in low and middle income countries. It is one of the top ten reasons in adult deaths. The global estimate of adults with diabetes in 2000 was around 151 million. This increased by 88% until 2009 and reached 285 million. It is estimated that there will be 578 million adults with diabetes by 2030 and 700 million adults by 2045 (IDF, 2019). Diabetes affects not only the patient but also the family and the social environment in which they live for a long time.

Diabetes are divided into three main groups: type 1 diabetes (T1D), type 2 diabetes mellitus (T2D) and gestational diabetes mellitus (GDM). Despite significant advances in the treatment of T1D diabetes, maintaining good glycemic control without hypoglycemia remains a problem for patients of all ages and healthcare providers (Bekiari et al. 2018). T2D diabetes is a condition in which blood sugar rises due to the inability of the pancreas to release enough insulin in cases such as stress, surgery, pregnancy or excess weight in people over the age of 40, or because the secreted insulin is not used adequately. The incidence of T2D is higher and 90% of people with diabetes have Type 2 diabetes (Davies et al. 2018). GDM is the first glucose intolerance that occurs during pregnancy and is one of the most common metabolic diseases in pregnancy (IDF, 2009). Type 1 and 2 diabetes are heterogeneous diseases in which the clinical presentation and disease progression can differ significantly. Classifying type 1 or type 2 diabetes is essential for determining treatment, but some individuals cannot be classified at the time of diagnosis. The traditional paradigms that type 2 diabetes occurs only in adults and type 1 diabetes only occurs in children are no longer accurate, as both diseases occur in both age groups (Rewers et al. 2015; Alonso et al. 2020; Jensen et al. 2021; ElSayed et al. 2023).

Kim et al. (2023) aimed to estimate mortality trends due to chronic liver disease in people with diabetes before and during COVID-19 (Kim et al. 2023). Ibrahim and Derbew (2023) applied supervised machine learning algorithms to classify and predict Type 2 diabetes disease status (Ibrahim and Derbew 2023). Liu et al. (2023) conducted a study to investigate the potential causal connection between non-alcoholic fatty liver disease and complications in type 1 diabetes and type 2 diabetes (Liu et al. 2023). In this study, it was aimed to examine the risk situations of complication development in diabetic patients. Therefore, logistic regression analysis was preferred among statistical analysis methods. Although logistic regression analysis has the same purpose as other regression models, it categorically provides the selection of the most compatible model for the dependent variable (Walker and Duncan 1967). While creating the data set, features such as age, gender, fasting glucose, postprandial blood sugar, HbA1C, HDL, VLDL, LDL, cholesterol, and triglyceride were selected. Our aim is to estimate the

risk of complications in the most accurate way by measuring the relationship between complication conditions and clinical outcomes in patients with diabetes.

## 2. Materials and Method

### 2.1. Data Collecting

Between January 2015 and December 2015, 10481 cases diagnosed as diabetes admitted to Gazi University Health Research and Application Center (GÜSAUM) Diabetes and Obesity Center on an outpatient or inpatient basis were analyzed retrospectively. The main diagnosis of diabetes and 1954 patients with complications related to diabetes were determined. Age, sex, fasting glucose, postprandial blood sugar, HbA1C, HDL, VLDL, LDL, cholesterol and triglyceride values were recorded for these 1954 cases. The remaining 8527 patients were evaluated with the same diagnosis and were not included in the study due to deficiencies in laboratory findings.

### 2.2. Statistical Analysis

In logistic regression and other statistical analysis of this study, SPSS 21 software was preferred. The significance level was accepted as  $\alpha = 0.05$  in all statistical analyzes. Binary and multinomial logistic regression (LR) analysis were used to find complication possibilities of patients with diabetes. If the LR dependent variable is binary, sequential or multinomial, it is a method used to reveal the cause-effect relationship between the dependent variable and independent variables. It is not only a method in which statistical significance of independent variables is evaluated as a risk factor, but also an analysis method that provides the possibility to calculate the estimated relative risk (odds ratio) (Bonney, 1987; Zhang, 1999; Dawson and Trapp, 2004; Hebel and McCarter, 2011). In LR analysis, it is important to establish the correct model in the beginning. Modeling with incorrectly selected variables may produce statistically significant results, but these results may not make any clinical significance. Before starting multivariate analysis, in the first step, it is recommended to look at the results of univariate logistic regression analysis to be performed separately for each independent variable with two-state dependent variable. The validity of the model both medically and biologically is directly related to the selection of independent variables to be included in the analysis (Menard, 2002; Saracbası and Dolgun, 2015). In logistic regression models, the basic concept is logit. The ratio of odds coefficients to each other of the two different cases examined is given by

$$Odds = \frac{p}{1 - p}$$

where  $p$  represents the probability. This ratio is used to explain the effect of the dependent variable on independent variables (Gujarati, 1999; Mertler and Vannatta, 2005; Alpar, 2013).

Logistic regression in which the probability of undiagnosed complications is modeled by a logistic or log-probability transformation is given by

$$Logit(p_i) = \ln\left(\frac{p_i}{1 - p_i}\right) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_n x_n$$

where  $x_i$  are continuous or binary explanatory variables,  $\beta_i$  are the regression coefficients estimated using maximum likelihood methods (Hosmer and Lemeshow, 1989; Bland and Altman, 2000). When probability ( $p_i$ ) takes values below 0.5, logit ( $p_i$ ) is negative, when probability ( $p_i$ ) takes values over 0.5, logit ( $p_i$ ) takes positive values. As the probability value increases, the value of logit ( $p_i$ ) will increase.

## 3. Results

In our study, in which the risk levels of complication development in diabetic patients were examined, the information of 1954 patients subject to the study is given in Table 1. In this study, 827 (42.3%) of the patients were male and 1127 (57.7%) were female. It was observed that complications developed in 142 (7.3%) of these patients. When the condition of 142 patients was examined, kidney complications in 21 patients, eye complications in 17 patients, complications with ketoacidosis in 22 patients, neurological complications in 17 patients and peripheral circulatory disorders in 65 patients (45.7%) were observed. In addition, in Table 1, evaluation was made

according to the type of diagnosis of patients, that is, diabetes type. Therefore, the most common type of complication among both Type 1 and Type 2 diabetes patients is peripheral circulatory disorders. Other complications are broadly given in Table 1 according to the two types of diabetes.

**Table 1.** Distribution of findings of the research.

<b>Number of Patient (N=1954)</b>	<b>n</b>	<b>%</b>
<b>Gender</b>		
Male	827	42.3
Female	1127	57.7
<b>Diabetes Complication Experience</b>		
Complication (-)	1812	92.7
Complication (+)	142	7.3
<b>Complication Type</b>		
Kidney Complication (+)	21	14.8
Eye Complication (+)	17	12.0
Complication with Ketoacidosis (+)	22	15.5
Neurological Complication (+)	17	12.0
Peripheral Circulatory Complication (+)	65	45.7
<b>Type of Diagnosis</b>		
Type 1 DM (+)	163	8.3
Type 2 DM (+)	1791	91.7
<b>Type 1 DM (+)</b>		
Complication Situation(n=71)		
Kidney Complication (+)	13	18.3
Eye Complication (+)	6	8.5
Complication with Ketoacidosis (+)	14	19.7
Neurological Complication (+)	10	14.1
Peripheral Circulatory Complication (+)	28	39.4
<b>Type 2 DM (+)</b>		
Complication Situation (n=71)		
Kidney Complication (+)	8	11.3
Eye Complication (+)	11	15.5
Complication with Ketoacidosis (+)	8	11.3
Neurological Complication (+)	7	9.8
Peripheral Circulatory Complication (+)	37	52.1

**Table 2.** Examination of diabetic patients according to some factors in terms of complication development situation (undeveloped/developed).

	$\beta$	Standard Error	Wald	df	p	OR	95% Confidence Interval (CI)	
							Lower Limit	Upper Limit
Gender*	-0.634	0.238	7.120	1	0.008	0.530	0.333	0.845
Age	0.026	0.010	7.341	1	0.007	1.027	1.007	1.046
Fasting Glucose	0.000	0.002	0.026	1	0.872	1.000	0.995	1.004
Postprandial Blood Sugar	-0.001	0.002	0.329	1	0,566	0.999	0.996	1.002
HbA <sub>1C</sub>	0.399	0.067	35.886	1	0.000	1.490	1.308	1.698
Constant	-7.215	0.765	88.917	1	0.000	0.001		
CCR=95.8%			$\chi^2(8)=7.773, p=0.456$					

\* The reference category 'Male' patients were selected for gender.

In the logistic regression analysis model established based on complication development conditions (undeveloped / developed) in diabetic patients; The effects of factors such as gender, age, fasting glucose, postprandial blood sugar and HbA<sub>1C</sub> are shown in Table 2. The model, established with the complication development conditions of diabetic patients, has a 95.8% correct classification rate (CCR). Gender, age and HbA<sub>1C</sub> parameters appear to be effective on the model ( $p < 0.05$ ). According to Hosmer-Lemeshow test statistics, which is one of the  $\chi^2$  statistics, the model was found to be significant ( $\chi^2(8)=7.773; p=0.456$ ). According to LR analysis, odds ratio (OR) 53% and confidence interval (CI = 0.333-0.845) for reference sex, OR 2.7% for age and (CI=1.007-1.046), OR 49% for HbA<sub>1C</sub> and (CI=1.308-1.698). When the size of the  $\beta$  coefficients is analyzed, it is seen that the effect power of gender and HbA<sub>1C</sub> parameters are higher on the model.

**Table 3.** Examination of diabetic patients according to some factors in terms of complication development situation (undeveloped/developed).

	$\beta$	Standard Error	Wald	df	p	OR	95% Confidence Interval (CI)	
							Lower Limit	Upper Limit
Gender*	0.047	0.266	0.031	1	0.860	1.048	0.623	1.765
Age	0.028	0.010	7.686	1	0.006	1.028	1.008	1.049
HDL	-0.069	0.014	23.829	1	0.000	0.933	0.908	0.960
VLDL	-0.013	0.012	1.181	1	0.277	0.988	0.966	1.010
LDL	-0.005	0.007	0.463	1	0.496	0.995	0.981	1.009
Cholesterol	-0.003	0.007	0.158	1	0.691	0.997	0.983	1.011
Triglycerides	-0.004	0.002	2.813	1	0.093	0.996	0.992	1.001
Constant	0.157	0.898	0.030	1	0.861	1.170		
CCR=95.7%			$\chi^2(8)=15.393, p=0.052$					

\* The reference category 'Male' patients were selected for gender.

The effect of diabetic patients on complication development status (undeveloped / developed) in terms of gender, age, HDL, VLDL, LDL, cholesterol, triglyceride is shown in Table 3. The correct classification rate in the model created is 95.7%. Age and HDL parameters appear to be effective on the model ( $P < 0.05$ ). Hosmer-Lemeshow test statistics result show that the model is significant ( $\chi^2(8)=15.393; p=0.052$ ). The LR analysis results show OR

2.8% and (CI=1.008-1.049) for age, OR 93.3% and (CI = 0.908-0.960) for HDL. When the sizes of  $\beta$  coefficients are considered, it is determined that the most effective variable on the model is HDL.

**Table 4.** Investigation of diabetic patients according to some factors in terms of complications.

	$\beta$	Standard Error	Wald	df	p	OR	95% Confidence Interval (CI)	
							Lower Limit	Upper Limit
Gender*	0.034	0.326	0.011	1	0.917	1.035	0.546	1.961
Age	0.032	0.013	6.188	1	0.013	1.033	1.007	1.059
Fasting Glucose	0.004	0.003	1.344	1	0.246	1.044	0.997	1.011
Postprandial Blood Sugar	-0.001	0.002	0.249	1	0.618	0.999	0.994	1.003
HbA1C	0.252	0.111	5,181	1	0.023	1.286	1.036	1.598
HDL	-0.008	0.021	18.015	1	0.000	0.916	0.879	0.954
VLDL	-0.035	0.014	6.458	1	0.011	0.966	0.940	0.992
LDL	-0.022	0.013	2.948	1	0.086	0.978	0.953	1.003
Cholesterol	0.016	0.014	1,312	1	0.252	1.016	0.989	1.043
Triglycerides	-0.007	0.003	4.993	1	0.025	0.993	0.988	0.999
Constant	-2.425	1.323	3.357	1	0.067	0.089		
CCR=97.2%			$\chi^2(8)=1.278, p=0,996$					

\* The reference category 'Male' patients were selected for gender.

Complications of diabetic patients in terms of complications situation in factors such as gender, age, fasting glucose, postprandial blood sugar and HbA1C, HDL VLDL, LDL, cholesterol, triglycerides are shown in Table 4. Table 4 shows that the correct classification rate of the current model is 97.2%. Age, HbA1C, HDL VLDL, triglyceride parameters appear to be effective on the model ( $p < 0.05$ ). The obtained values ( $\chi^2(8)=1.278; p=0.996$ ) show that the model is significant according to the Hosmer-Lemeshow test statistics. According to the LR analysis, it was found the OR 3.3% and (CI=1.007-1.059) for age, OR 28.6% and (CI=1.036-1.598) for HbA1C, OR 91.6% and (CI=0.879-0.955) for HDL, OR 96.6% for VLDL and (CI=0.940-0.992), OR 99.3% for triglyceride and (CI=0.988-0.999). When  $\beta$  coefficients are analyzed according to their sizes, it is seen that the most effective variable on the model is HbA1C.

**Table 5.** Examination of Diabetic Patients According to Some Factors in Terms of Complication.

	$\beta$	Standard Error	Wald	df	p	OR	95% Confidence Interval (CI)	
							Lower Limit	Upper Limit
<b>Retinopathy</b>	Intercept	-2.944	3.314	0.789	1	0.374		
	Age	-0.006	0.042	0.019	1	0.890	0.994	0.916 1.079
	Fasting Glucose	-0.011	0.010	1.086	1	0.297	0.989	0.969 1.010
	Postprandial Blood Sugar	0.031	0.014	5.167	1	0.023	1.031	1.004 1.059
	HbA1C	-0.049	0.210	0.055	1	0.815	0.952	0.631 1.436
	Gender=0	-0.141	0.954	0.022	1	0.882	0.868	0.134 5.629
	Gender=1							
<b>Ketoacidosis</b>	Intercept	-5.469	3.302	2.744	1	0.098		
	Age	-0.063	0.040	2.526	1	0.112	0.939	0.868 1.015
	Fasting Glucose	-0.022	0.012	3.393	1	0.065	0.978	0.955 1.001
	Postprandial Blood Sugar	0.045	0.015	9.070	1	0.003	1.046	1.016 1.078
	HbA1C	0.494	0.238	4.305	1	0.038	1.639	1.028 2.614
	Gender=0	-1.484	1.181	1.579	1	0.209	0.227	0.022 2.294
	Gender=1							
<b>Neuropathy</b>	Intercept	-9.315	4.586	4.125	1	0.042		
	Age	0.085	0.055	2.395	1	0.122	1.089	0.978 1.212
	Fasting Glucose	-0.011	0.013	0.663	1	0.415	0.989	0.964 1.015
	Postprandial Blood Sugar	0.022	0.017	1.813	1	0.178	1.023	0.990 1.056
	HbA1C	0.102	0.232	0.193	1	0.660	1.107	0.703 1.746
	Gender=0	-0.206	1.230	0.028	1	0.867	0.814	0.073 9.068
	Gender=1							
<b>Peripheral Circulation disorder</b>	Intercept	-2.957	2.802	1.114	1	0.291		
	Age	0.003	0.036	0.006	1	0.938	1.003	0.934 1.076
	Fasting Glucose	-0.015	0.009	2.926	1	0.087	0.985	0.968 1.002
	Postprandial Blood Sugar	0.036	0.012	8.520	1	0.004	1.036	1.012 1.061
	HbA1C	-0.036	0.178	0.041	1	0.840	0.965	0.680 1.368
	Gender=0	0.441	0.810	0.296	1	0.586	1.554	0.318 7.605
	Gender=1							

$$\chi^2(20)=17.923, p=0.806$$

\* The reference category 'Male' patients were selected for gender.

Complication development conditions of diabetic patients in terms of factors such as gender, age, fasting glucose, postprandial blood sugar and HbA<sub>1C</sub>, according to the types of complications (Retinopathy, Ketoacidosis, Neuropathy, Peripheral Circulatory Disorder) are shown in Table 5. According to LR results, the model is statistically significant ( $\chi^2(20)=17.923$ ;  $p=0.806$ ). Postprandial blood sugar for the development of complications of retinopathy, postprandial blood sugar for the development of complications of ketoacidosis, and HbA<sub>1C</sub>, postprandial blood sugar are effective parameters for the development of complication of peripheral circulatory disorders ( $p<0.05$ ). This information is also confirmed by examining the magnitudes of  $\beta$  coefficients in the complications of retinopathy, ketoacidosis, and peripheral circulatory disorders. It was determined as a postprandial blood glucose OR 3.1% for retinopathy complication and (CI=1.004-1.059), postprandial blood glucose OR 4.6% for ketoacidosis complication, (CI=1.016-1.078) and HbA<sub>1C</sub> OR 63.9%, (CI=1.028-2.614). For the complication of peripheral circulatory disorders, the postprandial blood sugar was found OR 3.6% and (CI=1.012-1.061).

#### 4. Discussion and Conclusion

Despite medical advances, diabetes is a serious health problem that has reached alarming levels. The development of complications in patients evaluated with the diagnosis of diabetes carries significant risks for the patient.

In this study, gender is an important variable in terms of the risk of developing complications and women have 47% less risk of developing complications than men. Age and HbA<sub>1C</sub> have important effects on the model. While the risk of complications developing increases by 2.7% with each unit increase in age, the risk of complications increases with each unit increase of HbA<sub>1C</sub> value by 49.0%. (Table 2).

Ozcan (2002), reported that men are more susceptible to nephropathy complications than women (Ozcan, 2002). Women have a more regular lifestyle and diet than men and this reduces the risk of complications. LR analysis showed that age and HDL parameters are effective on the model. It is determined that the risk of developing diabetic complications in both women and men increases with the increase in age. When the age increases by one unit, the risk of developing complications increases by 2.8% while the risk of developing complications decreases by 6.7% as a result of increasing HDL value (Table 3).

When LR analysis results are analyzed in detail, it is seen that age, HbA<sub>1C</sub>, HDL, VLDL and Triglyceride parameters have a significant effect on the model. As the HDL, VLDL, LDL and Triglyceride values increase, the risk of developing complications decreases. If the age, HbA<sub>1C</sub>, HDL and VLDL are increased by one unit, the risk of developing complications increases by 3.3%, 28.6% and 8.4%, respectively. Increasing one unit of VLDL and triglyceride reduce the risk of complications by 3.4% and 0.7%, respectively (Table 4).

Park et al. (2017), showed that the average age of patients with diabetic foot complications was significantly higher than those without complications, but HDL, LDL and triglyceride levels were not significant predictors (Park et al. 2017). This study is consistent with Park et al. (2017) results. The reason for this may be the aging of the organism with the advancing age, prolonged diabetes duration and accompanying chronic diseases. HDL, VLDL, LDL and triglycerides results obtained in this study are not consistent with Park et al. (2017). This causes incompatibility; it can be shown that the social and economic levels of the patients in the data set are high, the disease conditions are monitored regularly, the food and beverage states are more controlled, and the blood levels are measured frequently.

It has been determined that the risk of complications will increase with increasing HbA<sub>1C</sub> value. Selim (2017), found that more complications (retinopathy, nephropathy, neuropathy) developed in diabetic patients with HbA<sub>1C</sub> values above 7 (Selim, 2017). In addition, the American Diabetes Association (2004) recommends that HbA<sub>1C</sub> value be below 7.0% in non-pregnant diabetic adults (American Diabetes Association 2004). Current study confirm this information. This situation can be interpreted as bad glycemic index level causing more damage to organs and body systems. In the first logistic regression model based on the complication status, gender, age and HbA<sub>1C</sub> parameters can be determined as statistically significant variables when gender, age, fasting glucose, postprandial blood sugar and HbA<sub>1C</sub> value were selected as explanatory variables. It can be said that gender, age and HbA<sub>1C</sub> variables are factors affecting the complication status. In the multinomial logistic regression model established according to the complication conditions, when the development status of the retinopathy complication is compared to those who develop nephropathy, only postprandial blood sugar is considered as a statistically significant variable. One unit increase in postprandial blood sugar compared to the nephropathy development status increases the risk of retinopathy complications by 3.1%. According to those who developed nephropathy, postprandial blood sugar and HbA<sub>1C</sub> values were found to be statistically significant in terms of the development of ketoacidosis complication. One unit increase in postprandial blood sugar compared to nephropathy increases the risk of ketoacidosis complication by 4.6%. One unit increase of HbA<sub>1C</sub> value according to nephropathy development status increases the risk of ketoacidosis complication by 63.9%. When the development of the complication of peripheral circulatory disorders in patients with nephropathy is examined, only postprandial blood sugar is considered as a statistically significant variable. Compared to those who developed nephropathy, one unit increase in postprandial blood sugar increases the risk of peripheral circulatory disorders complications by 3.6%. (Table 5).

The results of this study are very important for patients with diabetes and have an early warning feature. Precautions to be taken against the factors causing complication development will prevent patients with diabetes from experiencing more serious health problems. This will increase the life quality of diabetic patients.

This study was conducted retrospectively on patients who were evaluated with the diagnosis of diabetes in a university hospital. The fact that the patients were constantly followed-up and their controls were frequently performed in university hospitals had an impact on the results. Conducting the study in community-based health institutions will reveal the diabetes profile of the society more clearly. Studies using all of the laboratory data retrospectively will yield better results. Prospective studies using the features selected in this study will contribute to a better understanding of diabetes. In individuals with diabetes, age, gender, blood lipid levels and HbA<sub>1C</sub> values were observed to be important variables for complication development. For these, community-based



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trainings for diabetic patients can be organized to raise awareness of people about diabetes. Thus, complications can be prevented or eliminated.

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