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Evaluation of microvascular complications in patients with new diagnosis type 2 diabetes

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Abstract. – OBJECTIVE: The incidence of microvascular complications such as diabetic retinopathy, diabetic nephropathy and diabetic neuropathy has increased in newly diagnosed diabetes patients. The aim of this study was to determine the factors affecting the incidence of microvascular complications in newly diagnosed patients with type 2 diabetes.

PATIENTS AND METHODS: This study was conducted on 97 newly diagnosed type 2 DM patients who applied to Malatya Training and Research Hospital Endocrinology outpatient clinic between September 2021 and July 2022. The patient files were reviewed retrospectively and their age, height, weight, body mass index (BMI), fasting/postprandial blood glucose measurements, serum HDL cholesterol, LDL cholesterol, total cholesterol, triglyceride, HbA1c levels, glomerular filtration rate (GFR) and complications of retinopathy, nephropathy, and neuropathy were recorded. Mann-Whitney U, *t*-test, Kruskal-Wallis, Binary logistic regression analysis, and Chi-square analysis were used to analyze the data.

RESULTS: The mean age of the patients included in the study was 47.40±7.78 (min: 23 - max: 62). Non-proliferative retinopathy was observed in 74.2% of patients, proliferative retinopathy in 25.8%, diffuse neuropathy in 49.5% and mononeuropathy was detected in 9.3% of them. Fasting blood glucose, postprandial blood glucose and HbA1c values were found to be higher in patients with proliferative retinopathy than in patients without retinopathy. Fasting blood glucose, postprandial blood glucose and HbA1c values were found to be higher in patients with neuropathy than in patients without neuropathy. In addition, patients with mononeuropathy had statistically significantly higher HbA1c values than patients with diffuse-type neuropathy. It was found that the urine protein values of patients with mononeuropathy were significantly higher than those without neuropathy and those with diffuse neuropathy. Each 0.677-unit increase in HbA1c increases the risk of proliferative retinopathy 1.98-fold, and every 1.018-unit increase increases the risk of neuropathy 2.76-fold. Proliferative retinopathy and mononeuropathy rates were discovered to be higher in patients with a family history.

CONCLUSIONS: Microvascular complications are common in newly diagnosed T2DM patients and an increase in HbA1c is a significant risk factor. Every newly diagnosed T2DM patient should be screened for microvascular complications.

Key Words:
Type 2 DM, Nephropathy, Neuropathy, Retinopathy.

Introduction

Diabetes Mellitus is a metabolic disease characterized by hyperglycemia, which occurs as a result of insufficient insulin secretion and/or decreased tissue response to insulin, resulting from the combination of genetic and environmental factors, as well as lifestyle changes. Inadequate insulin action on target tissues causes carbohydrate, fat and protein metabolism disorders. Insulin resistance or the lack of effect of insulin in people with type 2 diabetes (T2DM) significantly affects many organs and systems in the body due to hyperglycemia[1]. In addition to the acute effects of hyperglycemia, chronic microvascular (diabetic nephropathy, neuropathy, retinopathy) and macrovascular (cerebrovascular, cardiovascular, peripheral vascular) complications that have emerged over the years are also extremely crucial. Today, it is aimed to provide an ideal glucose regulation and to prevent the development of microvascular and macrovascular complications with close follow-ups[2]. The incidence of microvascular complications such as diabetic retinopathy, diabetic nephropathy and diabetic neuropathy has increased in newly diagnosed diabetes patients. These complications result in irreversible repercussions, reduce the patients' quality of life, shorten their lifespan, and cause labor and

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economic losses. It is important to evaluate the incidence of microvascular complications in newly diagnosed diabetes patients and to ensure that the necessary precautions are taken to prevent the negative consequences of diabetes. The chance of blindness, kidney failure and amputations that may develop due to microvascular complications can be reduced by early screening, regular blood sugar and blood pressure checks[3]. The aim of this study is to determine the factors affecting the incidence of microvascular complications in newly diagnosed diabetes patients.

Patients and Methods

This study was conducted on newly diagnosed T2DM patients who applied to Malatya Training and Research Hospital Endocrinology outpatient clinic between September 2021 and July 2022. Patients who applied within the specified time frame and satisfied the inclusion criteria were included in the study. The minimum number of people to be included was 86 in the sample size analysis, which was referenced as 80 power 5% confidence interval p=012 d=0.1. 97 people were reached in our study. Patients newly diagnosed with T2DM, between the ages of 18-75 and that did not meet the exclusion criteria were included in the study. During pregnancy and lactation, those younger than 18 years or older than 75, those with acute disease or infection at the time of enrollment, those with renal disease other than diabetic nephropathy, those using oral contraceptives and aspirin, those with hematological disease, those with thyroid dysfunction, those with known malignancies, those receiving chemotherapy and/or radiotherapy were not included in our study. The patient files were reviewed retrospectively by the researchers and their age, height, weight, body mass index (BMI), fasting/postprandial blood glucose measurements, serum HDL cholesterol, LDL cholesterol, total cholesterol, Triglyceride, HbA1c levels, glomerular filtration rate (GFR) and complications of retinopathy, nephropathy, neuropathy are noted.

In order to identify diabetic retinopathy, fundus examination was performed by an ophthalmologist with a 66 lens and slit lamp biomicroscope.

Identification of diabetic neuropathy, as well as examination and electromyography (EMG) were performed by a neurologist. Electrophysiological examinations were performed with the Nihon Kohden EMG device. Median, ulnar, radial, peroneal, tibial, sural and superficial motor and sensory nerve conductions were measured in at least three, usually four, extremities. Recording electrodes for motor conduction and ring electrodes for sensory nerve conduction were used and studied antidromically.

Diabetic nephropathy was determined by analyzing the microalbumin, glomerular filtration rate (GFR) and serum creatinine level in 24-hour urine samples. The samples were collected from all patients from 08:00 in the morning to 08:00 in the next day, and microalbumin and creatinine levels were measured. Microalbumin and creatinine levels in the urine were studied using the Integra 800 device by enzymatic colorimetric method in the biochemistry laboratory. In terms of microalbuminuria, 30-300 mg/day values were evaluated as positive. Glomerular filtration rate was calculated with the formula for creatinine clearance (24-hour urine creatinine × 24-hour urine volume/serum creatinine × 1,440).

Statistical Analysis

SPSS 22 program was used in the analysis of the data (IBM Corp., Armonk, NY, USA). The Kolmogorov test as a normal distribution test and the Smirnov test was used. Data are presented in the form of numbers, percentages, arithmetic mean, and standard deviation. Mann-Whitney U, t-test, Kruskal-Wallis, Binary logistic regression analysis (Forward LR model), Chi-square analysis were used in the analysis. A p-value of <0.05 was considered statistically significant.

Results

The mean age of 97 DM patients included in the study was 47.40±7.78 years (min: 23 - max: 62). Non-proliferative retinopathy was observed in 74.2% (n=72) of patients, proliferative retinopathy in 25.8% (n=25), diffuse neuropathy in 49.5% (n=48) and mononeuropathy was detected in 9.3% (n=9) of them. The sociodemographic characteristics of the patients and the distribution of microvascular complications are given in Table I.

When the metabolic parameters of the patients were compared according to the retinopathy type, it was found that the fasting blood glucose, postprandial blood glucose and HbA1c values of the patients with proliferative retinopathy were statistically significantly higher (Table II).

Table I. Sociodemographic characteristics and complications of the patients.

Gender	N	%
Male	38	39.2
Woman	59	60.8
Family history		
No	43	44.3
Yes	54	55.7
Cigarette		
No	59	60.8
Yes	38	39.2
Retinopathy		
Non-proliferative		
Light	4	4.1
Middle	20	20.6
Severe	26	26.8
Very severe	22	22.7
Proliferative		
Early	14	14.4
High risk	8	8.2
Severe	2	2.1
Clinically insignificant macular edema	1	1.0
Neuropathy		
No	40	41.2
Diffuse neuropathy		
Distal symmetrical	35	36.1
Autonomic neuropathy	13	13.4
Mononeuropathy		
Isolated peripheral involvement	7	7.2
Mono neuritis multiplex	2	2.1
Total	97	100.0

Upon comparing metabolic parameters of patients according to the neuropathy type, it was discovered that fasting blood glucose, postprandial blood glucose and HbA1c values were statistically significantly higher in patients with both types of neuropathies than those without neuropathy. In addition, patients with mononeuropathy had HbA1c values significantly higher than patients with diffuse type neuropathy. It was found that the urine protein values of patients with mononeuropathy were significantly higher in patients without neuropathy and those with the diffuse type (Table III).

Logistic regression models were found to be important to predict the risk of proliferative retinopathy and neuropathy in patients. Two different models were developed, which included factors such as age, weight, body mass index (BMI), fasting/postprandial blood glucose measurements, serum HDL cholesterol, LDL cholesterol, total cholesterol, triglyceride, HbA1c levels, and glomerular filtration rate. Analyses were made using the forward LR model. The risk of proliferative retinopathy increases 1.011-fold for every 0.011-unit increase in fasting blood glucose, and 1.98-fold for every 0.677-unit increase in HbA1c. In the model created with the same variables for neuropathy risk, it was found that the HbA1c variable had a substantial contribution, and each 1.018-unit increase increased the neuropathy risk 2.76 times (Table IV).

Table II. Comparison of metabolic parameters according to retinopathy type.

	Retinopathy						
	Non-proliferative retinopathy			Proliferative retinopathyl			
	Mean	SD	Median	Mean	SD	Median	p
Fasting blood glucose (mg/dL)	212.08	54.26	212.0	286.32	67.49	301.0	< 0.001
Postprandial blood glucose (mg/dL)	285.33	58.56	291.0	350.48	74.90	345.0	< 0.001
HbA1c (%)	8.44	1.05	8.3	10.196	1.66	9.9	< 0.001
Total Cholesterol (mg/dL)	205.50	32.28	205.0	207.76	30.61	209.0	0.804
LDL (mg/dL)	113.74	24.79	108.0	108.08	21.58	112.0	0.391
HDL (mg/dL)	43.37	10.13	41.5	42.12	11.53	42.0	0.415
TG (mg/dL)	230.97	63.14	232.5	239.68	71.09	236.0	0.310
Insulin (IU/mL)	15.56	3.68	15.95	15.17	3.02	14.5	0.632
Weight (kg)	84.64	9.96	84.0	86.28	13.27	83.0	0.518
BMI (kg/m^2)	35.86	3.78	36.20	36.024	4.98	36.7	0.870
GFR (mL/min)	94.97	19.00	94.0	98.20	23.28	96.0	0.458
Urine Protein	0.46	0.47	0.31	1.264			
	1.68	0.31	0.653				

HbA1c: Hemoglobin A1c, LDL: HDL: Low Density Lipoprotein, High Density Lipoprotein, TG: Triglyceride, BMI: Body Mass Index, GFR: Glomerular Filtration Rate.

Table III. Comparison of metabolic parameters according to neuropathy type.

	Neuropathy									
	No			Diffuse			Mononeuropathy			
	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	*p*
Fasting blood glucose (mg/dL)	197.83	45.81	189.00	246.35	65.87	236.00	298.89	69.02	312.00	< 0.001
Post prandial blood glucose (mg/dL)	271.75	53.65	272.50	315.58	69.93	312.00	365.33	64.48	398.00	< 0.001
HbA1c (%)	8.12	0.74	8.20	9.03	1.24	9.00	11.66	1.34	11.20	< 0.001
Total Cholesterol (mg/dL)	203.83	30.00	203.00	207.58	31.88	212.00	208.11	40.88	199.00	0.652
LDL (mg/dL)	116.20	22.86	111.50	109.37	24.18	106.50	110.33	28.52	109.00	0.551
HDL (mg/dL)	41.93	7.57	41.00	43.77	11.06	44.00	44.22	17.47	38.00	0.541
TG (mg/dL)	244.75	67.69	234.00	234.21	57.88	235.00	176.67	66.61	195.00	0.075
Insulin (IU/mL)	15.26	3.71	14.80	15.72	3.39	15.80	15.04	3.63	14.20	0.717
Weight (kg)	82.90	7.73	82.50	86.10	11.68	84.50	89.11	16.60	83.00	0.388
BMI (kg/m^2)	35.45	3.02	35.50	36.36	4.40	37.15	35.56	6.40	36.70	0.284
GFR (mL/min)	100.48	21.04	97.00	93.25	20.00	88.50	88.67	11.97	95.00	0.163
Urine Protein	0.42	0.34	0.31	0.60	0.90	0.30	2.16	1.97	0.80	0.010

HbA1c: Hemoglobin A1c, LDL: HDL: Low Density Lipoprotein, High Density Lipoprotein, TG: Triglyceride, BMI: Body Mass Index, GFR: Glomerular Filtration Rate.

Table IV. Proliferative logistic regression analyzes for retinopathy and neuropathy prediction.

Models		B	p	OR	95% CI for OR	
					Lower	Upper
Proliferative Retinopathy	FBG	0.011	0.044	1.011	1.000	1.023
	HbA1c	0.677	0.012	1.968	1.158	3.345
Neuropathy	HbA1c	1.018	< 0.001	2.769	1.681	4.559

HbA1c: Hemoglobin A1c, LDL: HDL: Low Density Lipoprotein, High Density Lipoprotein, TG: Triglyceride, BMI: Body Mass Index, GFR: Glomerular Filtration Rate.

When the frequency of microvascular complications was compared according to the presence of a family history, the rates of proliferative retinopathy and mononeuropathy were found to be statistically significantly higher in patients with a family history (Table V).

Discussion

Diabetes mellitus is a common metabolic disease and is associated with chronic, long-term macro-microvascular complications. The onset of T2DM (T2DM) is usually asymptomatic and the diagnosis may take many years. The estimated time for diagnosis is at least 4-7 years and, as a result, 30-50% of patients may remain undiagnosed[4]. The pathogenesis of complications in diabetes mellitus is not fully understood and its occurrence in some patients but not in others is a matter of debate. Usually at the time of T2DM diagnosis, the patient has developed at least one of the related complications. Microvascular complications from T2DM are common, and many studies[5-8] show that early detection and identification of risk factors for complications (retinopathy, nephropathy, and neuropathy) can delay or prevent progression to blindness, end-stage renal disease, and diabetic foot ulcers, respectively.

In this study, the frequency of microvascular complications and influencing factors in newly diagnosed T2DM patients were investigated. In our study, non-proliferative retinopathy was found in 74.2% of the patients, proliferative retinopathy in 25.8%, diffuse neuropathy in 49.5%, and mononeuropathy in 9.3% at the time of diagnosis. When the metabolic parameters of the patients were compared according to the retinopathy type, it was found that the fasting blood glucose, postprandial blood glucose and HbA1c values of the patients with proliferative retinopathy were higher.

When the metabolic parameters of the patients were compared according to the neuropathy type, it was found that the fasting blood glucose, postprandial blood glucose and HbA1c values were higher in patients with both types of neuropathies than those without neuropathy. In addition, patients with mononeuropathy had significantly higher HbA1c values than patients with diffuse type-neuropathy. It was found that the urine protein values of patients with mononeuropathy were significantly higher in patients without neu-

Table V. Comparison of microvascular complications according to family history.

	Family history		p
	No	Yes	
Retinopathy			
Non-proliferative	38 (88.4)	34 (63.0)	0.009
Proliferative	5 (11.6)	20 (37.0)	
Neuropathy			
No	25 (58.1)*	15 (27.8)*	0.004
Diffuse	17 (39.5)	31 (57.4)	
Mononeuropathy	1 (2.3)*	8 (14.8)*	

*< 0.05.

ropathy and those with the diffuse type. The risk of proliferative retinopathy increases 1.011-fold for every 0.011-unit increase in fasting blood glucose, and 1.98-fold for every 0.677-unit increase in HbA1c. Each 1.018 unit increase in HbA1c increases the risk of neuropathy by 2.76 times. The rates of proliferative retinopathy and mononeuropathy were found to be significantly higher in patients with a family history.

In the study conducted by Khanam et al[3] on 400 T2DM patients, the prevalence of diabetic retinopathy, nephropathy, and neuropathy was found to be 12.3%, 21.3% and 16.8%, respectively. In the logistic regression model, increasing age, being female, living in a rural area, increasing HbA1c and fasting blood glucose (FBG), and blood pressure were found to be significant, independent risk factors for any of the three microvascular complications. In this study, it was observed that all microvascular complications developed in the patients from the first three years after diagnosis. Increasing age, HbA1c, FBG, postprandial blood glucose (PPBG) and blood pressure are important risk factors for all kinds of microvascular complications[3].

Bansal et al[9] identified a prevalence of 18.04% for any microvascular illness in newly diagnosed T2DM diabetes mellitus complications. Neuropathy, retinopathy and nephropathy prevalence was found to be 8.2%, 9.5% and 2.8%, respectively. Triglycerides and old age were significantly associated with all complications. Triglycerides are significantly associated with neuropathy (OR: 1.01; p=0.05) and retinopathy (OR: 1.01; p = 0.02), while being male poses an increased risk for nephropathy.

In his study, Raman et al[10] found the prevalence of any microvascular complication to be 30.2%, the prevalence of diabetic retinopathy to be 4.8%, and the prevalence of diabetic nephropathy and neuropathy as 10.5% in newly diagnosed T2DM patients. Risk factors for the development of any microvascular complication were found to be increasing age, increased systolic blood pressure, and increased hemoglobin.

Ali et al[11] divided newly diagnosed DM patients into two groups: Group I with good glycemic control (HbA1c <6.5) and Group II with poor glycemic control (HbA1c >6.5). The frequency of microvascular complications in Group II was 89.8%. The prevalence of neuropathy, nephropathy and retinopathy was 68.5%, 56.2% and 31.4%, respectively. These percentages were 50%, 0%, and 31%, respectively, and significantly lower in Group I. In the study, it has been shown that the frequency of microvascular complications is much higher in patients with newly diagnosed T2DM who have poor glycemic control compared to those with average glycemic control. In our study, it was found that HbA1C is an important risk factor for the development of important microvascular complications. Therefore, ensuring tight glycemic control in newly diagnosed T2DM patients is extremely crucial to prevent and minimize the occurrence of complications. Kumar et al[12] found peripheral sensory neuropathy in 37%, nephropathy in 20%, and retinopathy in 17% of the study population in their study. Microvascular complications are seen in 48% of the study population. Increasing age, long duration of diabetes and high HbA1c were found to be common risk factors for all complications[12].

Pradeepa et al[13], in another study, found retinopathy in 17.5%, neuropathy in 25.7%, nephropathy in 5.1%, and microalbuminuria in 26.5% of the patients. Common risk factors identified for all three microvascular complications of diabetes were age, glycosylated hemoglobin, duration of diabetes, and serum triglycerides. A study by Kärvestedt et al[14] found that the prevalence of peripheral sensory neuropathy rose with severity of retinopathy (intermediate frequency 50% and severe or 100% in proliferative retinopathy). In multivariate analyses, FBG was independently associated with age, male gender, and HDL cholesterol, but not with the duration of diabetes or HbA1c.

Diabetic nephropathy and retinopathy affect approximately 25% of patients with T2DM; diabetic neuropathy occurs in almost 50% of the diabetic population. T2DM duration together with glucose, lipid and blood pressure values have been reported[15] as common risk factors for the development of these complications.

In a meta-analysis of 23 studies[16] involving 269,691 participants, the overall pooled prevalence of diabetic peripheral neuropathy was found to be 46%. In one study, the overall prevalence of microvascular complications was found to be 52.1% in 390 T2DM patients. Peripheral neuropathy (44.9%) had the highest prevalence among microvascular complications, followed by nephropathy (12.1%) and diabetic foot (7.2%). Multiple logistic regression analysis[17] revealed that a high HbA1c level, low education, high postprandial blood glucose, hypertension, abdominal obesity were significantly associated with an increased risk of vascular complications of diabetes.

In the study conducted by Agrawal et al[18] 32.5% of 11,157 individuals had retinopathy, 30.2% had nephropathy, and 26.8% had peripheral neuropathy. After conducting multiple logistic regression analysis, it was found that age had a significant correlation with retinopathy and neuropathy, and diabetes duration had a significant correlation with neuropathy and nephropathy. Higher HbA1c increases the risk of retinopathy, neuropathy and nephropathy[18]. Early detection of microvascular complications associated with T2DM is important as early intervention leads to better outcomes. However, awareness of their definition, prevalence and diagnostic methods are required. These results suggest that regular screening for microvascular complications should be performed.

Conclusions

According to the findings of our study, non-proliferative retinopathy was found in 74.2% of the patients, proliferative retinopathy in 25.8%, diffuse neuropathy in 49.5%, and mononeuropathy in 9.3%. Fasting blood glucose, postprandial blood glucose and HbA1c values were found to be greater in patients with proliferative retinopathy and neuropathy. Patients with mononeuropathy had significantly higher HbA1c values compared to patients with diffuse type neuropathy. It was found that the urine protein values of patients with mononeuropathy were significantly greater in patients without neuropathy and those with diffuse. Each 0.677-unit increase in HbA1c increases the risk of proliferative retinopathy 1.98-fold, whilst every 1.018-unit increase increases the risk of neuropathy 2.76-fold. It was found that the rates of proliferative retinopathy and mononeuropathy were significantly greater in patients with a family history. These results suggest that regular screening for microvascular complications should be performed, and every newly diagnosed T2DM patient should be screened for microvascular complications.

Conflict of Interest
The Authors declare that they have no conflict of interests.

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Informed Consent
Before beginning the survey, all respondents read the written permission form and voluntarily consented to participate.

Ethics Approval
Approval of the study was obtained with the decision of Turgut Ozal University Ethics Committee meeting with number 2022/125, dated 26/07/2022.

Authors' Contribution
The study design; B.Y, L.K data collection; L.Z and data analysis under the supervision of B.Y.; L.K. data interpretation and manuscript writing; B.Y.; L.K. and L.K. review and editing; B.Y.; L.K. and B.Y supervision and project administration. All authors approved the final version of the manuscript.

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