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ORIGINAL ARTICLE – OPEN ACCESS

Is There a Relationship Between Microvascular Complications and the Severity of Type 2 Diabetes Mellitus?

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ABSTRACT

Objective: The aim of this study was to determine the relationship between microvascular Type 2 diabetes mellitus (T2DM) complications and the severity and duration of diabetes in the light of sociodemographic and lifestyle variables.

Materials and Methods: This is a prospective cohort study based on 899 (527 females, 372 males) patients with T2DM aged 25–70 years. Patient information including socio-demographic variables; body mass index (BMI); lifestyle habits and duration of diabetes; treatment of diabetes; values for hemoglobin A1c (HbA1c); development of diabetes complications; and the presence of neuropathy, nephropathy, and retinopathy were recorded. A univariate and multivariate statistical analysis were performed.

Results: Significant differences were found between diabetics with HbA1c ≤7 and >7 in terms of the education level, occupation, household income, duration of diabetes, the number of children, smoking, physical exercise, eating fast food, control regularity, and diabetes education. A total of 17.1% of patients had diabetic retinopathy, 17.0% had neuropathy, and 13.7% had nephropathy. Among diabetics, 2.3% had three microvascular complications, whereas 66.6% had none of them. The prevalence of diabetes complications was lower in patients who had good glycemic control than those who had poor glycemic control. Furthermore, the highest reduction in the level of HbA1c was for sulfonylurea usage.

Conclusion: A high prevalence of diabetes complications is a burden for both the patients and the health care system. Screening, early diagnosis, management of the glucose level, and the follow-up may result in delayed diabetes complications.

Keywords: Diabetes, severity of type 2 diabetes, microvascular complications

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INTRODUCTION

Diabetes is a chronic and pandemic metabolic disease that needs a continuous medical care (1). Irregular dietary habits, poor physical activity, and stress enhance the occurrence of diabetes. The prevalence of diabetes is increasing, and it will grow from 285 million people in 2010 to 592 million in 2035 (2), and 629 million in 2045 (3). Moreover, the prevalence of diabetes among the people aged ≥20 in Turkey was calculated as 7.2% in 2002 (4), 12.7% in 2011 (5), and 16.5% in 2013 (6). According to these studies, the prevalence of diabetes increased by approximately 80%–100% in the recent 10 years.

Being overweight, having a medical history of diabetes, increasing age, a sedentary lifestyle, ethnicity, and uncontrolled blood glucose are diabetes risk factors. Diabetes has microvascular (small blood vessels damage) and macrovascular (arterial) complications (7). It leads to several physical symptoms, including ocular, renal, and neural complications among diabetic patients (8).

The optimum blood glucose level has been determined if HbA1c is smaller than 7% by the American Diabetes Association (ADA) (9). International Diabetes Federation (10) and American Association of Clinical Endocrinologists (11) has set HbA1c to ≤6.5% as the optimum level. Optimum glycemic control can decrease the risk of microvascular complications by decreased HbA1c level from 7.9% with an intensive treatment to 7% with conventional treatment (12, 13). Therefore, there was a 25% decrease in the overall microvascular complication rate (12, 13). In the world, 12% of total health care costs cover diabetes (3). Moreover, 75% of diabetic patients live in low- and middle-income counties. Controlled complications can reduce morbidity, mortality, and health expenditures (14).

Diabetes complications increase and the quality of life decreases due to the lack of glycemic control among patients with Type 2 diabetes in Turkey. The present study aimed to determine the relationship between microvascular diabetes complications, and the severity and duration of diabetes in the light of properties, and lifestyle habits.

MATERIALS and METHODS

This prospective cohort study was conducted at the Istanbul Medipol University Hospital and Istanbul Training and Research Hospital between September 2017 and July 2018. The age of the study subjects ranged between 25 and 70 years. Criteria for not selecting the subjects were as follows: Patients with gestational diabetes, Type 1 diabetes, and any physiological disorders. The sample size was determined by considering 17%–20% prevalence of impaired fasting glucose in Turkey (15), assuming the 0.1% level of significance, and 2% bound on the error of estimation, the minimum sample size required for this study was 1,250 subjects. A total of 1,250 subjects were approached; 899 (71.9%) gave their consent and were included. One of the outstanding strengths of this study was a large sample size in comparison with other studies.

Information such as patients' age, gender, family history of diabetes, height, weight, the level of HbA1c, and the complications of diabetes was obtained using a questionnaire. The level of average HbA1c ≤7% and >7% was considered as good and poor glycemic control, respectively. Diabetes and its complications were diagnosed based on the ADA criteria (1). The existence of retinopathy, neuropathy, and nephropathy was revealed by the responses of participants, because it was not possible to determine them using the biochemical results. Moreover, it was only evaluated whether these complications occurred or not. Ethical approval for the present study was received from the International Faculty of Medicine, İstanbul Medipol University (24.02.2016-124).

Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 22) software. The Kolmogorov–Smirnov test, a histogram, the Q–Q plot, and a box plot were used to control the normality of data (16–18). Student's t-test was used to ascertain the significant difference between the two means of a continuous variable (16–18). A The chi-squared test of independence (two-tailed), also called Pearson's chi-squared test, was performed to test for differences in the proportions of categorical variables between two or more groups for each variable (16–18). A multiple logistic regression analysis with the enter method was used to determine factors such as HbA1c, BMI, occupation, the level of income, and education associated with binary categorical variables as diabetic nephropathy, neuropathy, and retinopathy. It was performed to predict the presence or absence of these complications based on values of a set of independent variables. The Hosmer–Lemeshow test and classification table were used to show the goodness-of-fit to model. From the classification table, over 70% of correctly classified is expected for a good model fit. Moreover, small p-values for the Hosmer–Lemeshow test of the goodness-of-fit suggest that the model is a good fit to data as p>0.05. Expected values were calculated by model. The model is better fit to data for smaller differences between observed and expected values (19). Furthermore, Bonferroni corrections were used for the chi-square test of the table larger than 2*2. A p-value <0.05 was considered as the cut-off value indicating significance.

RESULTS

Table 1 represents socio-demographic characteristics and lifestyles of patients with T2DM in terms of the level of HbA1c. Out of 899 patients, 372 (41.4%) were males, and 527 (58.6%) were females. The mean age was 49.52±11.46 for males and 46.51±12.29 for females. The mean age of sample was 47.75±12.04, and the mean duration of diabetes was 8.36±5.42. The mean of height, weight, and body mass index was 166±8.86 cm, 77.98±13.14 kg, and 28.33±4.63 kg/m^2, respectively. Diabetes treatment was diet only for 29.3% patients, oral antidiabetic medications (OAD) only for 34.6% patients, insulin only for 22.4%, and OAD medications + insulin in 27.7% patients. Significant differences were found between well and poorly controlled diabetic patients in terms of the education level (p<0.001), occupation (p<0.001), household income status (p<0.001), duration of diabetes (p=0.001), the number of children (p=0.002), smoking (p<0.001), physical exercise (p<0.001), fast-food eating (p<0.001), regular control (p<0.001), and diabetes education (p<0.001).

Table 2 illustrates diabetic complications among patients with Type 2 diabetes considering several selected variables. A total of17.1% of patients had diabetic retinopathy, 17.0% had neuropathy, and 13.7% had nephropathy. Figure 1 indicates the prevalence of microvascular complications. Among diabetics, 2.3% had three microvascular complications, whereas 66.6% had none. Regarding to Table 2, the prevalence of diabetes complications was lower in patients who had good glycemic control than in those with poor glycemic control. Moreover, the significant differences were found among patients with diabetic retinopathy (p=0.013), neuropathy (p=0.032), and nephropathy (p=0.036) by the severity of diabetes. There was a significant difference between retinopathy and duration of diabetes (p<0.001), level of education (p<0.001), household income (p<0.001), physical activity (p=0.005), and smoking (p=0.011). Furthermore, neuropathy and duration of diabetes (p<0.001), the level of education (p=0.007), household income (p<0.001), and physical activity (p=0.001) havhade significant differences.

Table 3 denotes the multiple logistic regression with the enter method to determine the effects of HbA1c, BMI, occupation,the level of income and education on retinopathy, neuropathy, and nephropathy. The Nagelkerke R2 counted that the model accounted for almost 8% of variance for retinopathy and nephropathy, and for nearly 10% of variance for neuropathy. Results of the Omnibus tests indicated that the level of significance was 0.000 for retinopathy and neuropathy and 0.006 for nephropathy, which is <0.05, and it showed a better model. From the classification table, more than 70% correctly classified is expected for a good model of fit. 82.9%, 83%, 86.3% of subjects were correctly classified by the model for retinopathy, neuropathy, and nephropathy, respectively. They were the overall predictive accuracy. The significance values of the Hosmer–Lemeshow test for all conditions were >0.05, so it meant the good fit of the final model to data. Regarding regression, retinopathy was significantly associated with the level of HbA1c, education, and household income. The level of HbA1c and education, income, occupation, and BMI were significant predictors of neuropathy. HbA1c and BMI were made significant contributions to the model.

The final models for retinopathy, neuropathy, and nephropathy are indicated in Table 3:

Ln(Retinopathy)=3.374–1.629*HbA1c+0.298*Income+ 0.302*Education

Table 1. Sociodemographic and lifestyle properties of diabetic patients considering the level of HbA1c (n=899)

	Overall		HbA1c≤7% n=82(9.1%)		HbA1c>7% n=817(90.9%)		X^2	p
	n	%	n	%	n	%		
Age group								
<40	239	26.6	20	24.4	219	26.8	5.617	0.132
40–49	235	26.1	29	35.4	206	25.2		
50–59	249	27.7	23	28.0	226	27.7		
≥60	176	19.6	10	12.2	166	20.3		
Gender								
Female	527	58.6	40	48.8	487	59.6	3.602	0.058
Male	372	41.4	42	51.2	330	40.4		
Body mass index								
<25 (kg/m²)	205	22.8	15	18.3	190	23.3	5.173	0.075
25–29.9 (kg/m²)	400	44.5	31	37.8	369	45.2		
≥30 (kg/m²)	294	32.7	36	43.9	258	31.6		
Level of education								
Primary	209	23.2	57	69.5	188	23.0	83.342	**<0.001**
Secondary	193	21.5	13	16.0	180	22.0		
High school	214	23.8	4	4.9	210	25.7		
University	247	27.5	8	9.6	239	29.3		
Occupation								
Retired\housewife	229	25.5	49	59.8	180	22.0	60.793	**<0.001**
Officer	365	40.6	14	17.1	351	43.0		
Manual worker	198	22.0	17	20.7	181	22.2		
Businessman	107	11.9	2	2.4	105	12.9		
Household income (TL)								
Low	179	19.9	26	31.7	153	18.7	21.701	**<0.001**
Medium	570	63.4	56	68.3	514	62.9		
High	150	16.7	0	0	150	18.4		
Number of child								
0–1	138	15.3	15	18.3	123	15.1	12.209	**0.002**
2–3	602	67.0	42	51.2	560	68.5		
≥4	159	17.7	25	30.5	134	16.4		
Cigarette smoking								
None	521	58.0	22	26.8	499	61.1	51.038	**<0.001**
Smoker	219	24.4	24	29.3	195	23.9		
Ex-smoker	159	17.7	36	43.9	123	15.1		
Physical exercise								
Yes	200	22.2	3	3.7	197	24.1	18.024	**<0.001**
No	699	77.8	79	96.3	620	75.9		
Eating fast-food								
Never	226	25.1	33	40.2	193	23.6	20.232	**<0.001**
Daily	139	15.5	1	1.2	138	16.9		
Weekly	205	22.8	17	20.7	188	23.0		
Monthly	329	36.6	31	37.8	298	36.5		
Duration of diabetes								
1–5 years	302	33.6	42	51.2	260	31.8	14.323	**0.001**
6–10 years	365	40.6	29	35.4	336	41.1		
>10 years	232	25.8	11	13.4	221	27.1		
Regularly control								
Yes	711	79.1	51	62.2	660	80.8	15.568	**<0.001**
No	188	20.9	31	37.8	157	19.2		
Diabetes education								
Yes	320	35.6	16	19.5	304	37.2	10.181	**0.001**
No	579	64.4	66	80.5	513	62.8		

Table 2. Diabetes complications among patients with type 2 diabetes considering several variables

	Retinopathy					Neuropathy					Nephropathy				
	with 154(17.1%)		without 745(82.9%)		p	with 153(17.0%)		without 746(83.0%)		p	with 123(13.7%)		without 776(86.3%)		p
	n	%	n	%		n	%	n	%		n	%	n	%	
HbA1c															
≤7%	6	3.9	76	10.2	**0.013**	7	4.6	75	10.1	**0.032**	5	4.1	77	9.9	**0.036**
>7%	148	96.1	669	89.8		146	95.4	671	89.9		118	95.9	699	90.1	
Body mass index															
<25 (kg/m²)	29	18.8	176	23.6		24	15.7	181	24.3		14	11.4	191	24.6	
25–29.9 (kg/m²)	63	40.9	337	45.2	0.079	58	37.9	342	45.8	**<0.001**	67	54.5	333	42.9	**0.003**
≥30 (kg/m²)	62	40.3	232	31.1		71	46.4	223	29.9		42	34.1	252	32.5	
Diabetes duration															
1–5 years	36	23.4	266	35.7		38	24.8	264	35.4		31	25.2	271	34.9	
6–10 years	56	36.4	309	41.5	**<0.001**	50	32.7	315	42.2	**<0.001**	43	35.0	322	41.5	**0.001**
>10 years	62	40.3	170	22.8		65	42.5	167	22.4		49	39.8	183	23.6	
Level of education															
Primary	65	42.2	180	24.2		59	38.6	186	24.9		41	33.3	204	26.3	
Secondary	30	19.5	163	21.9	**<0.001**	30	19.6	163	21.8	**0.007**	20	16.3	173	22.3	0.289
High school	29	18.8	185	24.8		31	20.3	183	24.5		29	23.6	185	23.8	
University	30	19.5	217	29.1		33	21.5	214	28.7		33	26.8	214	27.6	
Household income															
Low	58	37.7	121	16.2		59	38.6	120	16.1		40	32.5	139	17.9	
Medium	72	46.8	498	66.8	**<0.001**	74	48.4	496	66.5	**<0.001**	58	47.2	512	66.0	**<0.001**
High	24	15.6	126	16.9		20	13.1	130	17.4		25	20.3	125	16.1	
Physical activity															
Yes	65	42.2	227	30.5	**0.005**	67	43.8	225	30.2	**0.001**	46	37.4	246	31.7	0.210
No	9	57.8	518	69.5		86	56.2	521	69.8		77	62.6	530	68.3	
Cigarette smoking															
None	75	48.7	446	59.9		84	54.9	437	58.6		62	50.4	459	59.1	0.080
Smoker	40	26.0	179	24.0	**0.011**	32	20.9	187	25.1	0.061	31	25.2	188	24.2	0.080
Ex-smoker	39	25.3	120	16.1		37	24.2	122	16.4		30	24.4	129	16.6	

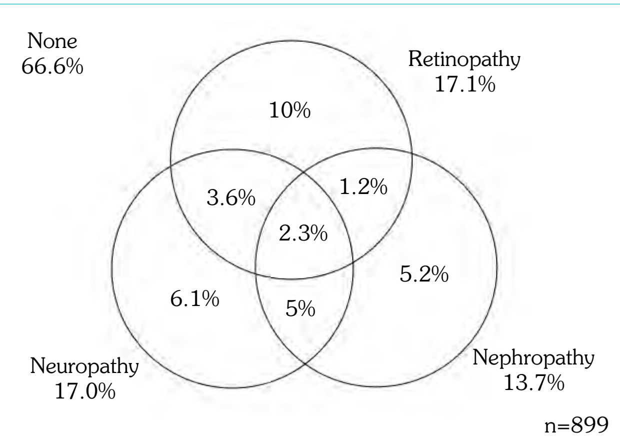

Figure 1. Prevalence of retinopathy, neuropathy, and nephropathy in diabetics

Ln(Neuropathy)=3.309–1.555*HbA1c–0.466*BMI+0.238*Occupation+ 0.379*Income+0.187*Education

Ln(Nephropathy)=4.137–1.187*HbA1c–0.293*BMI.

Figure 2 presents the mean reduction in the level of HbA1c in terms of the type of treatment. The mean reduction in HbA1c was –1.63±1.15 for the treatment with metformin. 47.3% of diabetics used it. The highest reduction was in treatment with sulfonylureas, and its value was –1.88±1.22.

DISCUSSION

Diabetes is one of the major metabolic diseases that result in short- and long-term complications. These complications burden health care systemsthe, society, and economy, both in low-income and high-income countries.

Table 3. Multiple logistic regression to examine variables associated with retinopathy, neuropathy, and nephropathy

	β	OR (95% CI)	p
Retinopathy			
Constant	3.374	29.216	**<0.001**
HbA1c	-1.629	0.196 (0.081–0.476)	**0.002**
Income	0.298	1.348 (1.901–1.665)	**0.006**
Level of education	0.302	1.353 (1.140–1.605)	**0.001**
Neuropathy			
Constant	3.309	27.375	**<0.001**
HbA1c	-1.555	0.211 (0.091–0.490)	**<0.001**
BMI	-0.466	0.627 (0.484–0.812)	**<0.001**
Occupation	0.238	1.269 (1.023–1.574)	**0.030**
Income	0.379	1.461 (1.179–1.812)	**0.001**
Level of education	0.187	1.206 (1.016–1.432)	**0.032**
Nephropathy			
Constant	4.137	62.637	**<0.001**
HbA1c	-1.187	0.305 (0.117–0.797)	**0.015**
BMI	-0.293	0.746 (0.570–0.977)	**0.033**

OR: Odd ratios; CI: Confidence interval; BMI: Body mass index

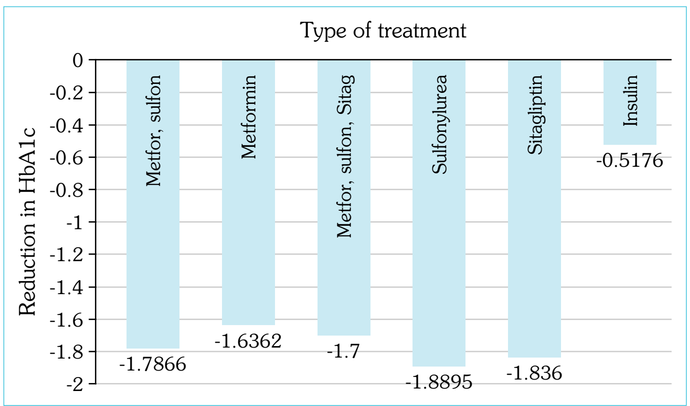

Figure 2. Mean reduction in the level of hba1c regarding the type of treatment

This study reported that 17.1%, 17.0%, and 13.7% of patients had retinopathy, neuropathy, and nephropathy, respectively. In the same vein, Liu et al. indicated that 14.8% of patients had retinopathy, 17.8% had neuropathy, and 10.7% had nephropathy (20). As reported by Bener et al., the prevalence of retinopathy was 13.6%, of neuropathy 10.3%, and of nephropathy 12.7% (21), while 23.4% had kidney-disease-related diabetes (22). The prevalence of all three microvascular complications was nearly 30% (23). The percentage of patients with retinopathy, neuropathy, and nephropathy was 8.1% in Tunisia (24), 15% in Canada (25), and 11.5% in the United Kingdom (26), respectively.

Patients aged 40–49 and 50–59 years are more likely to have a poor glycemic control than other age groups. It is consisted that diabetic patients aged >40 years were at risk of poor glycemic control (27). An advanced age increases diabetes-related complications (8). Moreover, the type of treatment shows an alteration in the HbA1c level. Metformin is the most widely used oral antidiabetic drug. It might be effective to use not only an oral antidiabetic, but also combinations of two or more such medications. Due to the fluctuation in the HbA1c level, the number of medications may be increased, and it may decrease the adaptation to medicine. Therefore, the HbA1c level may not be regulated (28).

The level of HbA1c increased renal complications by approximately 6 times. Furthermore, a prolonged diabetes duration leads to increased renal complications (29). Good glycemic control reduces microvascular complications related to diabetes. In a follow-up study, the level of glucose was put under control with intensive treatment, and it decreased retinopathy in the united States (30). Our study found that the level of education and income and all three microvascular complications were significantly associated. Furthermore, the prevalence of a low education level was high in patients with a low level of HbA1c. Education plays an important role in the HbA1c level regulation as patients have knowledge about their eating and drinking habits, physical exercise, and treatment process. The frequency of measuring blood glucose levels leads to a better diabetes management, prevention of diabetic complications (31), and a decreased burden of diabetes.

Oral antidiabetics help in reducing the level of HbA1c. Our study found that sulfonylureas lead to a greatest decrease in the level of HbA1c. The study calculated that the reduction in HbA1c from baseline was −0.83% with sitagliptin, −1.30% with metformin, and −2.07% with sitagliptin and metformin (32). The HbA1c level was decreased with sulfonylurea monotherapy by the ratio 1.5% on average, and with sulfonylurea, and other oral medications by 1.6%, compared with placebo groups (33). The present study results are in agreement with Flory et al.'s (2014) findings, which showed the largest initial decline in sulfonylureas (34).

A limitation of this study is that its design is a cross-sectional cohort study. Due its nature, a longitudinal study might have been more efficient in acquiring data about diabetes complications. An additional uncontrolled factor is selection bias despite the spurt of the interviewers. Moreover, data were collected only among patients with T2DM who visited clinics, and not among inpatients and patients who unable to visit hospitals. Lastly, characteristics and diabetes complications were elicited from patients' self-reports; therefore, this might have led to the recall bias. Despite its limitations, the study offers some insight regarding the association between the level of HbA1c and diabetes complications.

CONCLUSION

The most obvious finding from the present study is that the increased severity of diabetes also increases diabetes complications. A high prevalence of diabetes complications is a burden for patients and the health care system. Thus, a more extensive screening, early diagnosis, management of the glucose level, and follow-up may all lead to delayed diabetes complications.

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Author Contributions: Concept – FÇ, AB, MO; Design – FÇ, AB, MO; Supervision – FÇ, AB; Resource – FÇ, AB, MO; Materials – FÇ, AB, MO; Data Collection and/or Processing – FÇ, AB, MO; Analysis and/or Interpretation – FÇ, AB; Literature Search – FÇ; Writing – FÇ, AB; Critical Reviews – FÇ, AB.

Conflict of Interest: The authors have no conflict of interest to declare.

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