

## ASSESSMENT OF PREVALENCE AND RISK FACTORS FOR DIABETIC RETINOPATHY IN PATIENTS WITH TYPE 1 AND TYPE 2 DIABETES EXAMINED AT A TERTIARY CARE

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### ABSTRACT

**Introduction:** Diabetic retinopathy (DR) is a microvascular complication of diabetes mellitus and the leading cause of visual impairment and blindness. The aim of the study was to estimate and compare the prevalence of DR and to determine an association between DR and systemic risk factors in hospitalized type 1 (DMT1) and type 2 (DMT2) diabetic patients.

**Material and methods:** We analyzed 260 patients with diabetes, 43 with DMT1 and 217 with DMT2. The following data were collected: age, gender, type and duration of diabetes, glycemic control, blood pressure, estimated glomerular filtration rate, ophthalmologic examinations and routine biochemical parameters.

**Results:** Out of the total number of 260 patients, 77 (29.6%) had non-proliferative DR (NPDR), 21 (8.1%) had proliferative DR (PDR), 29 (11.1%) had diabetic macular edema (DME), and 69 (23.5%) had diabetic cataracts. Forty-three (16.5%) patients were previously diagnosed with DMT1 and 217 (83.5%) with DMT2. The duration of diabetes was not significantly longer in DMT1 (12.8±11.2 years) in comparison to DMT2 (11.07±8.1 years). The prevalence of NPDR and PDR did not differ statistically in either groups. DME was more prevalent in DMT2 than in DMT1 (P<0.05). Diabetic cataract was found in 26.7% vs. 6.7% of patients with DMT2 and DMT1, respectively (p<0.01). The duration of diabetes significantly correlated with NPDR and PDR in DMT1 (r=0.31, p<0.05; r=0.55, p<0.001, respectively). In DMT2, significant correlations were found between the duration of diabetes and cataract, NPDR, PDR and DME (r=0.31, p<0.001; r=0.43 p<0.01, r=0.16 p<0.05 and r=0.20 p<0.01, respectively). Fasting plasma glucose (FPG) significantly correlated with PDR (r=0.258, p<0.05), while HbA1c with DME (r= 0.15 p<0.05).

**Conclusion:** The duration of diabetes and hyperglycemia were associated with DR in both types of diabetes.

**Keywords:** diabetic retinopathy, cataract, glycemic control, duration of diabetes

### INTRODUCTION

Retinopathy, nephropathy and neuropathy are unique microvascular complications of diabetes. Diabetic retinopathy (DR) is the most common

neuromicrovascular complication of diabetes. Cataract and other eye complications are more frequent in patients with diabetes. In general, diabetic

retinopathy advances from mild non-proliferative abnormalities to moderate and severe non-proliferative diabetic retinopathy (NPDR), then progressing to proliferative diabetic retinopathy (PDR), and/or diabetic macular edema (DME). The onset and progression of diabetic retinopathy may be without symptoms. For this reason, in newly diagnosed DMT2, about 20% of the patients may have DR. Regular screening and follow-up 5 years after the onset of diabetes have been recommended in adult patients with DMT1 and also at the time of diagnosis of DMT2. It is estimated that DR is the leading cause of visual impairment and blindness in adult diabetic patients of the working age group between 20 and 74 years of age. The prevalence of retinopathy and the vision-threatening type is estimated to be at 40.3% and 8.2%, respectively. Diabetic retinopathy currently affects 100 million people, with 17 million people with PDR, 21 million with DME, and 28 million people with vision threatening DR worldwide [1]. It is the sixth leading cause of blindness, and it is also an important cause for preventable blindness [2].

The pathophysiology of DR is complex and not fully clear. Many systemic risk factors have been associated with DR, especially the duration of diabetes and glycemic control. The duration of diabetes is a non-modifiable and well documented risk factor for the onset and progression of DR. Twenty years after the onset of diabetes mellitus type 1 (DMT1) almost all patients have DR, and 60% of patients with diabetes mellitus type 2 (DMT2) have retinopathy. Chronic hyperglycemia is a major risk factor for microvascular diabetic complications, including retinopathy, nephropathy and neuropathy. Tight glycemic control is considered the most important modifiable risk factor to reduce the development, progression of DR, and low rate of visual loss. Tight control of blood pressure in hypertensive patients with diabetes contributes to the decrease in the risk of the development and progression of diabetic retinopathy. Additional risk factors include nephropathy, dyslipidemia and obesity. Puberty, pregnancy, anemia, and tight glycemic control achieved for a short period are the causes for onset or worsening of the preexisting diabetic retinopathy.

The aim of this study was to estimate the prevalence of DR in diabetic patients and to determine an association between DR and various risk factors (duration of diabetes, glycemic control, glomerular filtration rate (GFR), lipids, systolic and

diastolic blood pressure, body mass index (BMI) and gender.

## MATERIALS AND METHODS

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This cross-section study used the medical records from the Hospital Department at the University Clinic of Endocrinology in Skopje. The hospital is equipped with well-established diabetes care. A total number of 260 diabetic patients were admitted to the hospital from January 2014 to September 2014. Medical records were reviewed, and the completed medical records were included in this study. These variables included the following data: age, gender, BMI, type and duration of diabetes, glycemic control with glycated hemoglobin (HbA1c), fasting plasma glucose (FPG), postprandial plasma glucose (PPG), estimated glomerular filtration rate (GFR) and blood pressure (systolic and diastolic). An ophthalmologist performed ophthalmologic examinations at the ophthalmologic unit at the same Clinic, using the classification scale of DR [3]. Patients with type 1 and type 2 diabetes were analyzed separately.

Fasting plasma glucose and PPG, within target levels of 7mmol/l and <10 mmol/l, respectively, were measured by using the glucose oxidase method. Serum HbA1c levels were measured by using ion-exchange high-performance liquid chromatography (HPLC). HbA1c levels less than 7% were considered the controlled target level according to the ADA recommendations [4]. The blood samples for lipoproteins were analyzed using Cobas Integra 700, according to standard methods. Total cholesterol and triglycerides were determined by full enzymatic methods (TH-CHOD-POD-PAP and triglycerides-GPO; Cobas Integra 700, Hoffmann-La Roche, Basel, Switzerland). HDL-C was measured by the polyanion precipitation method, while LDL-C was calculated using the Friedewald formula. Glomerular filtration rate was calculated using the National Kidney Foundation method. Diabetic retinopathy was considered as dependent variable, while independent variables were age, gender, duration of diabetes, HbA1c, FPG, PPG, cholesterol, LDL-C, HDL-C, and GFR.

Statistical analysis. The SPSS statistical package was used for statistical analyses. The differences between the two groups were tested using the t-test for independent variables. The Pearson

correlation test was used for statistical correlations between the analyzed variables.  $P < 0.05$  was considered statistically significant.

## RESULTS

Age, gender, BMI, duration of diabetes, blood pressure values, and routine biochemical parameters of all patients are shown in Table 1. The mean age of the analyzed patients was  $55.3 \pm 14.4$  years. Forty-three (16.5%) patients out of 260 had DMT1 and 217 (83.5%) patients had DMT2. Seventy seven patients (29.6%) had NPDR, from which 20% mild, 6.9% moderate, and 2.7% severe form of NPDR. Twenty one patients (8.1%) had PDR, 29 (11.1%) had DME, and 69 (23.5%) had diabetic cataract (Table 1). The average values of lipids showed dyslipidemia (Table 1). The systolic and diastolic average blood pressures were evaluated.

**Table 1.** Anthropometric and biochemical parameters of the included patients

variables	Average value $\pm$ SD
Age (years)	$55.3 \pm 14.4$
BMI (kg/m <sup>2</sup> )	$29.8 \pm 6.0$
Duration of DMT1 (years)	$12.8 \pm 11.1$
Duration of DMT2 (years)	$11.2 \pm 8.1$
HbA1c (%)	$9.8 \pm 1.9$
FPG (mmol/L)	$9.9 \pm 4.2$
PPG (mmol/L)	$11.5 \pm 4.3$
Cataract	61/260 (23.5%)
NPDR	mild 52/260 (20%); moderate 18/260 (6.9%); severe 7/260 (2.7%)
PDR	21/260 (8.1%)
DME	29/260 (11.1%)
GFR (ml/m <sup>2</sup> )	$113.8 \pm 40$
T.Ch (mmol/L)	$4.84 \pm 1.4$
TG (mmol/L)	$2.08 \pm 1.5$
HDL-C (mmol/L)	$1.16 \pm 0.5$
LDL-C (mmol/L)	$3.11 \pm 2.2$
T.Ch/HDL-C	$5.08 \pm 3.8$
LDL-C/HDL-C	$3.02 \pm 2.7$
SP (mmHg)	$134.2 \pm 21.8$
DP (mmHg)	$80.5 \pm 14.2$

Abbreviations. BMI: body mass index; DMT1: type 1 diabetes mellitus; DMT2: type 2 diabetes mellitus; HbA1c: glycosylated hemoglobin; FPG: fasting plasma glucose; PPG: post-prandial glucose; NPDR: non-proliferative diabetic retinopathy; PDR: proliferative dia-

betic retinopathy; DME: diabetic macular edema; GFR: glomerular filtration rate; T.Ch: total cholesterol; TG: triglycerides; HDL-C: high density cholesterol; LDL-C: low-density cholesterol; SP: systolic blood pressure; DP: diastolic blood pressure.

According to age, patients with DMT1 were younger in comparison to DMT2 ( $36.8 \pm 14.6$  years &  $58.3 \pm 11.2$  years, respectively), with a statistically significant difference ( $p < 0.001$ ). The duration of diabetes was longer in DMT1 ( $12.8 \pm 11.2$  years) in comparison to DMT2 ( $11.07 \pm 8.1$  years), without a statistical difference. HbA1c and FPG did not differ statistically between two groups. Only PPG was statistically significantly lower in DMT1 in comparison to DMT2 ( $p < 0.01$ ). In other metabolic parameters, the mean level of HDL-C was lower in DMT2 in comparison to DMT1 ( $p < 0.01$ ). LDL-C/HDL-C ratio and SP were higher in DMT2 compared to DMT1, ( $p < 0.05$ ). The prevalence of NPDR was higher in DMT2 and PDR was higher in DMT1, but without a statistically significant difference. When grading according to the severity of NPDR, the mild form of NPDR had 77.8 vs. 66.2%, the moderate form had 22.2 vs. 23.5%, and the severe form had 0 vs. 10.3% of DMT1 and DMT2 patients, respectively. DME was more prevalent in DMT2 than in DMT1, with a statistical difference ( $p < 0.05$ ). Diabetic cataract was found in 26.7% of patients with DMT2 and 6.7% in DMT1, with a statistical difference ( $p < 0.01$ ).

The duration of diabetes significantly correlated with NPDR and PDR in DMT1 ( $r = 0.31$ ,  $p < 0.05$ ;  $r = 0.55$ ,  $p < 0.001$ , respectively). In DMT2, significant correlations were found between the duration of diabetes and cataract, NPDRP, PDR, DME ( $r = 0.31$ ,  $p < 0.001$ ;  $r = 0.43$ ,  $p < 0.01$ ,  $r = 0.16$ ,  $p < 0.05$  and  $r = 0.20$ ,  $p < 0.01$ , respectively) (Table 2). FPG significantly correlated with PDR ( $r = 0.258$ ,  $p < 0.05$ ), and PPG had near to a significant correlation with PDR ( $p = 0.07$ ). HbA1c significantly correlated with DME ( $r = 0.15$ ,  $p < 0.05$ ).

Other statistically significant correlations were observed between systolic and diastolic blood pressure and diabetic cataract ( $r = 0.24$ ,  $p < 0.01$  and  $r = 0.15$ ,  $p < 0.05$ , respectively). GFR had a statistically significant negative correlation with the duration of diabetes, PDR and diabetic cataract ( $r = -0.21$ ,  $p < 0.01$ ,  $r = -0.16$ ,  $p < 0.05$ , and  $r = -0.30$ ,  $p < 0.001$ ); positive correlation with FPG ( $r = 0.44$ ,  $p < 0.001$ ). PDR negatively correlated with HDL-C ( $r = -0.209$ ,  $p < 0.01$ ).

**Table 2.** Comparison of analyzed variables between DMT1 and DMT2 patients

	Type 1 DM (N=43)	Type 2 DM (N=217)	p value
sex (m:f)	21/22	79/138	NS
<b>age (yeras)</b>	<b>36.8±14.6</b>	<b>58.9±1.2</b>	<b>&lt;0.001</b>
<b>BMI (kg/m2)</b>	<b>25,6±5,3</b>	<b>30.6±5.9</b>	<b>&lt;0.01</b>
Duration of diabetes(years)	12.8±11.2	11.07±8.1	NS
HbA1c (%)	9.6±2.4	9.8±1.8	NS
FPG (mmol/L)	10.4±4.5	9.8±4.2	NS
<b>PPG (mmol/L)</b>	<b>7.2±3.9</b>	<b>11.9±4.2</b>	<b>&lt;0.05</b>
<b>Cataract</b>	<b>3/43 (6.9%)</b>	<b>58/217 (26.7%)</b>	<b>&lt;0.01</b>
NPDR	9/43 (20.9%) ( m i l d = 7 , moderate=2)	68/217 (31.3%) ( m i l d = 4 5 , moderate= 1 6 , severe=7)	NS
PDR	6/43 (13.9%)	15/217 (6.9%)	NS
<b>DME</b>	<b>1/43 (2.3%)</b>	<b>28/217 (12.9%)</b>	<b>&lt;0.05</b>
GFR (ml/m2)	120.18±42.9	112.6±39.6	NS
T.Ch (mmol/L)	4.7±0.9	4.8±1.4	NS
TG (mmol/L)	1.72±1.9	2.14±1.4	NS
<b>HDL-C (mmol/L)</b>	<b>1.42±0.6</b>	<b>1.11±0.46</b>	<b>&lt;0.01</b>
LDL-C (mmol/L)	2.8±0.9	3.15±2.35	NS
T.Ch/HDL-C	4.8±6.5	5.13±3.2	NS
<b>LDL-C/HDL-C</b>	<b>2.1±1.0</b>	<b>3.18±2.9</b>	<b>&lt;0.05</b>
<b>SP (mmHg)</b>	<b>125,6±21,9</b>	<b>135.9±21.4</b>	<b>&lt;0.05</b>
DP (mmHg)	76.5±10.5	81.3±14.7	NS

Abbreviations. BMI: body mass index; HbA1c: glycosylated hemoglobin; FPG: fasting plasma glucose; PPG: post-prandial glucose; NPDR: non-proliferative diabetic retinopathy; PDR: proliferative diabetic retinopathy; DME: diabetic macular edema; GFR: glomerular filtration rate; T.Ch: total cholesterol; TG: triglycerides; HDL-C: high density cholesterol; LDL-C: low-density cholesterol; SP: systolic blood pressure; DP: diastolic blood pressure.

## DISCUSSION

The prevalence of any DR and PDR in our population was 37.7% and 8.1%, respectively. This is lower compared to 47% in the Jerneld and Algvere study, and 34.1% in the Lemu Mersha et al. study [5, 6]. The data available in the literature are quite different. A pooled analysis of 22,896 people with diabetes from 35 population-based studies in the U.S., Australia, Europe, and Asia (between 1980–2008) showed that the overall prevalence of any DR and PDR (in T1DM and T2DM) was 34.6% and 7.5%, respectively [1]. The incidence and risk of progression of DR have markedly declined in the last years. The global prevalence of DR in 2021 was reported to be at 22.7% [7].

Previous studies confirmed that the duration of diabetes was a consistent risk factor for DR [8,

9]. It may be a predominant factor for determining the prevalence of DR. In patients with an age at diagnosis <30 years in the Wisconsin study [10], the frequency of any retinopathy approached 92% after 13-14 years of diabetes and 75% in the study of Henricsson et al. [11]. We did not divide patients according to age, but the percentages of DR in DMT1 and DMT2 were lower (34.8 and 38.2%, respectively) in our study. The lower percentage in our groups may be due to the lower duration of diabetes, twelve years in DMT1, and eleven years in DMT2. The duration of diabetes significantly correlated statistically with NPDR and PDR in DMT1, and with NPDR, PDR, DME, and diabetic cataract in DMT2 patients. The strength of correlation was higher in the DMT1 patients' group. The differences in the prevalence of DR between ours and other studies indicate that the occurrence of retinopathy is also influenced by factors other than the duration of the disease.

Glycemic control is one of the most important risk factors for DR, especially in DMT1. Hyperglycemia contributes to microvascular complications as well as to DR. The results of the Diabetic complication Control trials (DCCT) [12], UK Prospective Diabetes Study (UKPDS) [13], and Advanced (ACCORD) Eye Study [14] showed that intensive antidiabetic therapy reduces the risk of the development and progression of diabetic retinopathy. Total glycemic exposure was the major determinant that influenced retinopathy progression. Therefore, FPG, PPG and HbA1c had an impact on DR and DME. According to the HbA1c, our patients were poorly controlled, but still better than the Wisconsin study [10]. In our study, HbA1c positively correlated with DME. DMT1 and DMT2 patients had similar glycemic control and duration of diabetes, so the prevalence of DR was similar. There was a statistically significantly higher prevalence of diabetic cataracts in the DMT2 group (26.7 vs. 6.9%), which was expected, as the patients in this group were older. Also, the prevalence of DME was statistically significantly higher in the DMT2 group (12.9 vs. 2.3%). This can be explained as the DMT2 group patients were older and had statistically significantly higher PPG than the DMT1 group. HbA1c correlated significantly statistically with DME. Besides FPG, PPG, and HbA1c, glucose variability was proven to show a specific triggering effect on oxidative stress [15]. Further, in patients with DMT2, FPG variability was found to be a risk factor for DR, independently of the mean FPG or HbA1c [16]. This finding emphasizes the need for a reduction in glucose variability by more frequent glycemic measurements or continuous glucose monitoring (CGM), as a reliable glycemic control.

Many studies have investigated the effects of hypertension on DR. The lowering of blood pressure has a significant impact in the onset and progression of diabetic retinopathy, especially in people with DMT 2 [13]. UKPDS showed a reduction in DR and DME, with the lowering of systolic blood pressure from the mean of 154 mmHg to 144 mmHg [13]. Therefore, a systolic pressure of 120 mmHg did not show any additional beneficial effect, compared to 140 mmHg in a similar cohort of the ACCORD study [14]. Our results showed a statistically significant correlation between DME and diastolic blood pressure ( $r=0.17$   $p<0.05$ ). We cannot discuss previous regulation of blood pressure because this is a cross-sectional study. DMT2 patients were significantly older, and they had a significantly higher BMI compared to DMT1,

significantly higher systolic blood pressure, a significant correlation of DME with diastolic blood pressure, significantly lower HDL-C, significantly higher LDL-C/HDL-C and were characterized with higher percentage of DME and higher mean values of PPG.

Several observational studies have suggested that dyslipidemia may play a role in the progression of diabetic retinopathy [17-19]. Dyslipidemia is associated with retinal hard exudate and visual loss. The Australian Diabetes, Obesity and Lifestyle study [17] involving 11,247 adults from 42 areas of Australia did not show a significant association between serum lipids and DR. The recent meta-analyses [18] did not find any obvious differences in triglycerides, total cholesterol, and HDL-C levels between patients with DR and without DR. Slightly higher LDL-C levels were observed in the DR cases. We did not compare lipids between patients with and without DR. Dyslipidemia was more frequent in T2DM patients, but only HDL-C and LDL-C/HDL-C were statistically significantly different and there was a negative correlation between PDR and HDL-C. Correlations were estimated in all population groups, T1DM and T2DM. Patients with early stages of DR and high levels of triglycerides and low levels of HDL-C (such as in our study) may have protective benefits with fenofibrate therapy [20].

The association between DR and BMI is controversial. The underlying pathophysiological mechanisms supporting the association between higher BMI and DR are yet to be defined. Besides the aldose reductase activity and vascular endothelial growth factor (VEGF), metabolic syndrome and increased oxidative stress have also been suggested as possible pathophysiological mechanisms [21]. Most studies have reported a significant association between high BMI and obesity with DR [22-29]. Conversely, others have reported an association between low BMI and DR [30-32] suggesting a possible protective role for higher BMI in the development of DR. A recent meta-analysis [33] showed neither being overweight nor obesity were associated with an increased risk of DR. In this study, most of the patients with T1DM were overweight, and T2DM were obese. There were significant differences in BMI between the groups. Obesity in T2DM patients may be the reason for the high prevalence of DME and cataract, but these parameters did not have significant correlations. Significantly lower HDL-C and higher LDL-C/HDL-C levels, as well

as significantly higher systolic blood pressure and higher mean PPG values in DMT2 patients that were significantly older and heavier compared to DMT1 patients enabled higher percentage of ophthalmologic complications DME and NPDR.

The association between diabetic nephropathy and retinopathy was confirmed by our results. The GFR have a statistically significant negative correlation with the duration of diabetes, PDR, and diabetic cataract. A positive correlation was noted between GFR and FPG in all patients.

We confirm that the duration of diabetes is one of the most important factors for all forms of DR, and glycemic control, arterial blood pressure and GFR also exercise an influence on DR in T1DM and T2DM patients. This is the first large study in our country. Another study showed that the development of DR is influenced by four major factors, namely, sociodemographic characteristics, comorbidities, complications, and diabetic conditions [34]. The incidence of DR varies by region, so it is important to estimate the risk in every population. These findings highlight an opportunity for aggressive early risk factors modification. Patients with diabetes require regular follow-up with primary care physicians to optimize their glycemic, blood pressure and lipid control to prevent development and progression of DR and other diabetes-related complications [35]. Other risk factors of DR include higher body mass index, puberty and pregnancy, and associations with some genetic and inflammatory markers.).

## CONCLUSION

The duration of diabetes and hyperglycemia were associated with DR in both types of diabetes. An association between DR and declining renal function was found. The influence of obesity on DR was not an inconclusive finding.

DMT2 patients who were significantly older and heavier compared to DMT1, with significantly higher systolic blood pressure, lower HDL-C, higher LDL-C/HDL-C, higher mean PPG values, significant correlation of DME with diastolic blood pressure and duration of diabetes were characterized by a higher percentage of DME.

It is important for clinicians to encourage their patients to optimize glycemic control, blood pressure, lipids and their body weight in both

groups of diabetes for the prevention of diabetic ophthalmic complications.s.

## REFERENCES

1. Yau JW, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. Global prevalence and major risk factors of diabetic retinopathy. *Diabetes Care*. 2012;35:556-564.
2. World Health Organization. Global Initiative for the Elimination of Avoidable Blindness. WHO/PBL/97.61 Rev 2. 2006. [Last accessed on 2016 Jan 05]. Available from: [http://www.who.int/blindness/Vision2020\\_report.pdf](http://www.who.int/blindness/Vision2020_report.pdf)
3. Wilkinson CP, Ferris FL, Klein RE, Lee PP, Agardh CD, Davis M, Dills D, Kampik A, Pararajasegaram R, Verdager JT. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. *Ophthalmology*. 2003;110:1677-1682.
4. American Diabetes Association. Glycemic targets. *Diabetes Care* 2022;45(Supplement\_1):S83-S96.
5. Jerneld B, Algvare P. Relationship of duration and onset of diabetes to prevalence of diabetic retinopathy. *Am J Ophthalmol*. 1986;102(4):431-7.
6. lemu Mersha G, Alimaw YA, Woredekal AT. Prevalence of diabetic retinopathy among diabetic patients in Northwest Ethiopia—A cross sectional hospital based study. *PLoS ONE*. 2022;17(1):e0262664. <https://doi.org/10.1371/journal>.
7. Teo ZL, Tham YC, Yu M, Chee ML, Rim TH, Cheung N, Bikbov MM, Wang YX, Tang Y, Lu Y, et al. Global Prevalence of Diabetic Retinopathy and Projection of Burden through 2045: Systematic Review and Meta-analysis. *Ophthalmology* 2021;128:1580-1591.
8. Klein R, Klein BE, Moss SE, Davis MD, Demets DL. The Wisconsin Epidemiologic Study of Diabetic Retinopathy. II. Prevalence and risk of diabetic retinopathy when age at diagnosis is less than 30 years. *Arch Ophthalmol* 1984;102:520-526.
9. Sehnaz Karadeniza Z, Temel Yilmaz B. Duration of diabetes and prevalence of diabetic retinopathy: Istanbul Diabetic Retinopathy Study—IDRS results 1. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*. 2007;1(1):43-48.
10. Klein R, Knudtson MD, Lee KE, Gangnon R, Klein BE. The Wisconsin Epidemiologic Study of Diabetic Retinopathy: XXII the

- twenty-five-year progression of retinopathy in persons with type 1 diabetes. *Ophthalmology*. 2008;115(11):1859-68.
11. Henricsson M, Nilsson A, Groop L, Heijl A, Janzon L. Prevalence of diabetic retinopathy in relation to age at onset of the diabetes, treatment, duration and glycemic control. *Acta Ophthalmol Scand*. 1996;74(6):523-7.
  12. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993;329:977-986.
  13. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular care. *diabetes journals.org Solomon and Associates 417 and microvascular complications in type 2 diabetes: UKPDS 38*. *BMJ* 1998;317:703-71312.
  14. ACCORD Study Group, ACCORD Eye Study Group, Chew EY, et al. Effects of medical therapies on retinopathy progression in type 2 diabetes. *N Engl J Med*. 2010;363:233-244 .
  15. Monnier L, Mas E, Ginet C, et al. Activation of oxidative stress by acute glucose fluctuations compared with sustained chronic hyperglycemia in patients with type 2 diabetes. *JAMA*. 2006;295:1681-7.
  16. Takao T, Ide T, Yanagisawa H, et al. The effect of fasting plasma glucose variability on the risk of retinopathy in type 2 diabetic patients: retrospective long-term follow-up. *Diabetes Res Clin Pract*. 2010;89:296-302.
  17. Tapp RJ, Shaw JE, Harper CA, et al. The prevalence of and factors associated with diabetic retinopathy in the Australian population. *Diabetes Care* 2003;26:1731-7.
  18. Zhou Y, Wang C, Shi K and Yin X. Relationship between dyslipidemia and diabetic retinopathy. A systematic review and meta-analysis. *Medicine (Baltimore)*. 2018;97(36):e12283.
  19. Petrie JR, Guzik TJ, Touy RM. Diabetes, Hypertension, and Cardiovascular Disease: Clinical Insights and Vascular Mechanisms. *Can. J. Cardiol*. 2018;34,575-584.
  20. Keech AC, Mitchell P, Summanen PA, et al. FIELD study investigators. Effect of fenofibrate on the need for laser treatment for diabetic retinopathy (FIELD study): a randomised controlled trial. *Lancet* 2007;370:1687-1697.
  21. Kaštelan S, Tomić M, Gverović Antunica A, Ljubić S, Salopek Rabatić J, Karabatić M. Body Mass Index: A Risk Factor for Retinopathy in Type 2 Diabetic Patients'. *Mediators Inflamm*. 2013;436329. *Medicine (Baltimore)*. 2017;96(22):e6754.
  22. Henricsson M, Nyström L, Blohmé G, et al. The incidence of retinopathy 10 years after diagnosis in young adult people with diabetes: results from the nationwide population-based Diabetes Incidence Study in Sweden (DISS) *Diabetes Care*. 2003;26(2):349-354.
  23. Turner R. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UK-PDS 34) *The Lancet*. 1998;352(9131):854-865.
  24. Van Leiden HA, Dekker JM, Moll AC, et al. Risk factors for incident retinopathy in a diabetic and nondiabetic population: the Hoorn study. *Archives of Ophthalmology*. 2003;121(2):245-251.
  25. Dirani M, Xie J, Fenwick E, et al. Are obesity and anthropometry risk factors for diabetic retinopathy? The diabetes management project. *Investigative Ophthalmology & Visual Science*. 2011;52(7):4416-4421.
  26. Katušić D, Tomić M, Jukić T, et al. Obesity-a risk factor for diabetic retinopathy in type 2 diabetes? *Collegium Antropologicum*. 2005;29(supplement):47-50.
  27. Zhang L, Krzentowski G, Albert A, Lefebvre PJ. Risk of developing retinopathy in diabetes control and complications trial type 1 diabetic patients with good or poor metabolic control. *Diabetes Care*. 2001;24(7):1275-1279.
  28. Li X, Wang Z. Prevalence and incidence of retinopathy in elderly diabetic patients receiving early diagnosis and treatment. *Experimental and Therapeutic Medicine*. 2013;5(5):1393-1396.
  29. De Block CEM, De Leeuw IH, Van Gaal LF. Impact of overweight on chronic microvascular complications in type 1 diabetic patients. *Diabetes Care*. 2005;28(7):1649-1655.
  30. Lim LS, Shyong Tai E, Mitchell P, et al. C-reactive protein, body mass index, and diabetic retinopathy. *Investigative Ophthalmology and Visual Science*. 2010;51(9):4458-4463.
  31. Raman R, Rani PK, Gnanamoorthy P, Sudhir RR, Kumaramanikavel G, Sharma T. Association of obesity with diabetic retinopathy: Sankara neethralaya diabetic retinopathy epidemiology and molecular genetics study (SN-DREAMS Report no. 8) *Acta Diabetologica*. 2010;47(3):209-215.
  32. Dowse GK, Humphrey ARG, Collins VR, et al. Prevalence and risk factors for diabetic retinopathy in the multiethnic population of Mauritius. *American Journal of Epidemiology*. 1998;147(5):448-457.
  33. Zhou Y, Zhang Y, Shi K, Wang C. Body mass index and risk of diabetic retinopathy. A meta-analysis and systematic review. *Medicine (Baltimore)*. 2017;96(22):e6754
  34. Naserrudin NA, Jeffree MS, Kaur N, Rahim SSSA, Ibrahim MY. Study on the Development

of a Conceptual Framework to Identify the Risk Factors of Diabetic Retinopathy among Diabetic patients: A Concept Paper. *Int. J. Environ. Res. Public Health*. 2022;19:12426.

35. Sharon SD, Chew E, Duh E, Sabrin L, Sun KJ, Brain VL, Charles WC and Gardner WT. Diabetic Retinopathy : A Position statement by the American Diabetic Association. *Diabetes Care* 2017;40:412-418.

## Резиме

### ПРОЦЕНА НА ПРЕВАЛЕНЦИЈАТА И РИЗИК-ФАКТОРИТЕ ЗА ДИЈАБЕТИЧНА РЕТИНОПАТИЈА КАЈ ПАЦИЕНТИ СО ДИЈАБЕТЕС ТИП 1 И ТИП 2 ВО ТЕРЦИЈЕРНА УСТАНОВА

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**Вовед:** Дијабетичната ретинопатија (DR) е микроваскуларна компликација на дијабетес мелитус и водечка причина за оштетување на видот и за слепило. Целта на студијата беше да се процени и да се спореди преваленцијата на DR и да се утврди поврзаноста меѓу DR и системските фактори на ризик кај хоспитализираните пациенти со дијабетес тип 1 (DMT1) и тип 2 (DMT2) на терцијарна нега.

**Материјали и методи:** Анализиравме 260 пациенти со дијабетес, 43 со DMT1 и 217 со DMT2. Беа одредени следниве податоци: возраст, пол, тип и траење на дијабетесот, гликемиска контрола, крвен притисок, проценета стапка на гломеруларна филтрација, офталмолошки прегледи и рутински биохемиски параметри.

**Резултати:** Од вкупно 260 пациенти, 77 (29,6 %) имале непролиферативна DR (NPDR), 21 (8,1 %) имале пролиферативна DR (PDR), 29 (11,1 %) имале дијабетичен макуларен едем (DME) и 69 (23,5 %) имале дијабетичен катаракт. Четириесет и тројца пациенти (16,5 %) беа со DMT1 и 217 (83,5 %) со DMT2. Времетраењето на дијабетесот беше несигнификантно подолго кај DMT1 ( $12,8 \pm 11,2$  години) во споредба со DMT2 ( $11,07 \pm 8,1$  години). Преваленцијата на NPDR и PDR не се разликуваше статистички во двете групи. DME беше присутен кај DMT2 отколку кај DMT1 ( $p < 0,05$ ). Дијабетичен катаракт пронајдовме кај 26,7 % наспроти 6,7% од пациентите со DMT2 и DMT1, соодветно ( $p < 0,01$ ). Времетраењето на дијабетот статистички значајно корелираше со NPDR и PDR во DMT1 ( $r = 0,31, p < 0,05$ ;  $r = 0,55, p < 0,001$ , соодветно). Во DMT2 беа пронајдени статистички значајни корелации меѓу времетраењето на дијабетесот и катарактот, NPDR, PDR, и DME ( $r = 0,31, p < 0,001$ ;  $r = 0,43 p < 0,01$ ,  $r = 0,16 p < 0,05$  и  $r = 0,20 p < 0,01$ , соодветно). Плазма гликозата на гладно (FPG) статистички значајно корелираше со PDR ( $r = 0,258, p < 0,05$ ), додека HbA1c со DME ( $r = 0,15 p < 0,05$ ).

**Заклучок:** И кај двата типа дијабетес времетраењето и хипергликемијата беа асоцирани со DR..

**Клучни зборови:** дијабетична ретинопатија, катаракт, гликемиска контрола, времетраење на дијабетесот