Research Article

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The effect of cardiometabolic control and malnutrition on the prevalence and prognosis of diabetic retinopathy in type 2 diabetes

Tip 2 diyabette kardiyometabolik kontrol ve malnütrisyonun diyabetik retinopati prevalansı ve prognozuna etkisi

Melek Özdemir, Yaşar Dağ, Mehmet Uzunlulu, Aytekin Oğuz, Aylin Ardagil, Ömer Acar, Bensu Selbest

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Abstract

Purpose: This study aims to investigate the predictive value of cardiometabolic control, gamma glutamyl transferase (GGT) and malnutrition-related inflammation markers for predicting diabetic retinopathy (DR) prevalence and prognosis**.**

Materials and methods: Type 2 Diabetes Mellitus patients who were consecutively admitted to Internal and Ophthalmology outpatient clinics were included in this study. Clinical, haematological and biochemical data were recorded. Cut-off values of GGT, hemoglobin, albumin, lymphocyte and platelet (HALP) score, nutritional risk index (NRI) and prognostic nutritional index (PNI) scores were determined by receiver operator characteristic curve analysis. Univariate and multivariate analyses were performed to determine the association of all variables with DR. We evaluated which of these tests were predictive and prognostic for the development of DR.

Results: This study included 166 patients. Fasting blood glucose (p<0.001), creatinine (p=0.01), HbA1c (p<0.001) and microalbuminuria (p=0.01) were higher in patients with retinopathy. Mean arterial pressure (p=0.01), fasting blood glucose (p=0.03), triglyceride (p=0.008), body mass index (BMI) (p=0.02) and HbA1c (p=0.04) increased significantly as GGT level increased. Contrary to the literature, HALP, PNI and NRI scores were not associated with DR.

Conclusion: Duration of diabetes, cardiometabolic control and GGT level are variables with predictive value for the prognosis of DR. No significant correlation was found between malnutrition-related inflammation markers and DR development and stage.

Keywords: Diabetic retinopathy, cardiometabolic control, GGT, malnutrition releated inflamation markers.

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Öz

Amaç: Bu çalışmanın amacı kardiyometabolik kontrol, gama glutamil transferaz (GGT) ve malnütrisyonla ilişkili inflamasyon belirteçlerinin diyabetik retinopati (DR) prevalansı ve prognozunu öngörmedeki değerini araştırmaktır.

Gereç ve yöntem: Bu çalışmaya Dahiliye ve Göz Hastalıkları polikliniklerine ardışık olarak başvuran Tip 2 Diabetes Mellitus hastaları dahil edilmiştir. Klinik, hematolojik ve biyokimyasal veriler kaydedildi. Alıcı operatör karakteristik eğri analizi ile GGT, hemoglobin, albümin, lenfosit ve trombosit (HALP) skoru, nutrisyonel risk indeksi (NRI) ve prognostik nutrisyonel indeks (PNI) skorlarının cut-off değerleri belirlendi. Tüm değişkenlerin DR ile ilişkisini belirlemek için tek değişkenli ve çok değişkenli analizler yapıldı. Bu testlerden hangilerinin DR gelişimi için öngörücü ve prognostik olduğu değerlendirilmiştir.

Bulgular: Bu çalışmaya 166 Tip 2 Diyabetes Mellitus hastası dahil edildi. Retinopati olanlarda; açlık kan glukozu (p<0,001), kreatinin (p=0,01), HbA1c (p<0,001) ve mikroalbüminüri (p=0,01) yüksek bulundu. Hastaların GGT düzeyi arttıkça ortalama arteriyel basınç (p=0,01), açlık kan glukoz (p=0,03), trigliserit (p=0,008), vücut kütle indeksi (BMI) (p=0,02) ve HbA1c (p=0,04) değerlerinin anlamlı arttığı bulundu. Literatürün aksine HALP, PNI ve NRI skorun DR ile anlamlı ilişki saptanmadı.

Melek Özdemir, Ph.D. Pamukkale University, Faculty of Medicine, Department of Medical Oncology, Denizli, Türkiye, e-mail: melekozdemir@pau.edu.tr (https://orcid.org/0000-0003-1894-9743) (Corresponding Author)

Yaşar Dağ, M.D. Basaksehir Cam and Sakura City Hospital, Istanbul Istanbul, Türkiye, e-mail: dryasardag@gmail.com (https://orcid.org/0000-0002-0449-6600)

Mehmet Uzunlulu, Prof. Medeniyet University, Faculty of Medicine, Department of Internal Medicine Branch, Istanbul, Türkiye, e-mail: mehmetuzunlulu@yahoo.com (https://orcid.org/0000-0001-8754-1069)

Aytekin Oğuz, Prof. Istanbul Medeniyet University, Faculty of Medicine, Department of Internal Medicine Branch, Istanbul, Türkiye, e-mail: aytekinoguz@hotmail.com (https://orcid.org/0000-0002-2595-5167)

Aylin Ardagil, M.D. Dunya Eye Hospital, Istanbul, Türkiye, e-mail: aardagil@gmail.com (https://orcid.org/0000-0002-1849-6644)

Ömer Acar, Ph.D. Celal Bayar University, Faculty of Medicine, Department of Medical Oncology, Manisa, Türkiye, e-mail: dracaromer@gmail.com (https://orcid.org/0000-0003-4408-1976)

Bensu Selbest, Ph.D. Pamukkale University, Faculty of Medicine, Department of Internal Medicine, Denizli, Türkiye, e-mail: drbensuselbest@gmail.com (https://orcid.org/0009-0003-2159-9294)

Sonuç: Diyabet süresi, kardiyometabolik kontrol ve GGT düzeyi diyabetik retinopati prognozu için prediktif değeri olan değişkenlerdir. Malnütrisyonla ilişkili inflamasyon belirteçleri ile DR gelişimi ve evresi arasında anlamlı bir ilişki bulunmamıştır.

Anahtar kelimeler: Diyabetik retinopati, kardiyometabolik kontrol, GGT, malnutrisyon ilişkili inflamasyon belirteçleri.

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Introduction

The metabolic disorder of type 2 diabetes mellitus (type 2 DM) is a condition characterised by hyperglycaemia in which peripheral insulin resistance or impaired insulin secretion mechanisms are the cause. It is a chronic metabolic disorder requiring continuous medical care as a result of impaired efficient utilisation of carbohydrates, fats and proteins. In the pathogenesis, environmental factors such as obesity are blamed as well as the influence of genetic factors. It is estimated that diabetes affects 530 million people worldwide and DR is seen in 10.5 per cent of people aged 20-79 years. The majority of diabetes cases consist of type 2 DM patients. The increase in metabolic syndrome and obesity cases over the years also suggests that type 2 DM cases will increase. According to the World Health Organization, the number of people with diabetes is expected to reach 300 million by 2025.

Turkiye is a region where cases are increasing in proportion to its large surface area and increasing population and screening programmes are emphasised more. Increasing life expectancy, changes in lifestyle and deterioration in dietary habits increase the frequency of diabetes and diabetes-related complications. Glycosylation, abnormalities in lipid metabolism, chronic inflammatory state and oxidative system disorders are thought to be the causes of pathogenesis. Microvascular and macrovascular complications are main causes of morbidity and mortality in type 2 DM. Early diagnosis will provide early treatment and rehabilitation of chronic complications. As a result, we believe that the duration without complications due to diabetes will increase [1-3].

In the current literature, duration of diabetes was the strongest predictor of the prevalence of DR [4, 5]. In another study, Henricsson et al. [6] accepted glycaemic control as the risk factor of the most common. And defined other risk factors as high blood pressure, high hyperlipidaemia, increased oxidant stress, renal impairment and chronic inflammation [7]. In the current literature hypertension and dyslipidaemia are also defined as risk factors.

Since DR may be asymptomatic until the end of life, every patient with type 2 DM should undergo annual screening including visual acuity, intraocular pressure measurement, slit lamp and dilated fundus examination [8]. It will be too late as irreversible complications will develop after the symptoms occur. Microvascular and macrovascular complications can be prevented with early diagnosis and treatment.

GGT, which is the subject of internal medicine speciality thesis, is a glycoprotein membrane-bound peptidase enzyme. It is a transporter of gamma-glutamyl groups from gamma-glutamyl peptides to other peptides, water and amino acids. In the literature, studies show that elevated GGT levels negatively predict metabolic syndrome and cardiovascular disease [9-11]. Considering that it may have a predictive value in the prevalence of DR, it was included in this study. The pathogenesis of DR consists of steps including ischemia, cell damage, inflammatory response, disruption of the retinal-blood barrier and neovascularisation. Clinical studies have concluded that inflammation, immune response and nutrition predict the presence of DR [12].

In this study, the full text of the internal medicine speciality thesis on ‘The effect of GGT level and cardiometabolic risk factors on DR staging in type 2 DM patients. This clinical study was organised on the basis of the recorded data of the patients included in the internal medicine thesis, using current knowledge from the literature and predictive markers obtained from the recorded laboratory data. There are no new data records about the patients [11].

As prognostic markers to predict malnutrition, PNI, NRI and HALP scores were calculated. The incidence of microvascular and macrovascular complications increases with malnutrition and hypoglycaemia. The HALP score takes into account malnutrition, inflammation and anaemia. It has been shown in the literature to predict malignancy, cerebrovascular disease and heart failure [13-16]. The power of the PNI and the NRI, which are markers that allow us to measure malnutrition, to predict DR was investigated in this study. The prognostic nutritional index obtained from the serum albumin and the lymphocyte count was called the PNI [7, 17]. The nutritional risk index was calculated from albumin, weight, ideal weight and height. It was called NRI [17]. The relationship between malnutrition and the prevalence and severity of DR is not well understood. In this study, the predictive power of HALP, PNI and NRI score, defined in the literature as markers of malnutrition in clinical trials, to predict DR was calculated.

The predictive value of cardiometabolic control, malnutrition markers (HALP, PNI and NRI) and GGT levels in predicting DR development in type 2 DM was investigated. The etiology of microvascular complications of diabetes has been studied in the literature [18-22]. To the best of our knowledge, there has been no study on this topic and its content, and it is believed that this study will contribute to the literature.

Materials and methods

Study population

In this study, 166 consecutive type 2 DM patients who applied to Internal Medicine and Ophthalmology outpatient clinics between January-July 2014 were included. Ethics committee approval was obtained on 01.08.2013. The Declaration of Helsinki principles were followed throughout. The following were included: type 2 DM, age above 40 years, absence of DR in the control group and presence of DR in the study group. Exclusion criteria were alcohol use, drug use (paracetamol, phenytoin, TAD, phenobarbital), known acute or chronic hepatobiliary disease (cholangitis, cirrhosis), chronic renal failure and retinopathy caused by other causes (collagen tissue disease, radiation induced retinopathy, hypertension, malignancy). Detailed anamnesis was taken from the patients who had the study criteria and physical examination was performed.

Data collection and calculation of prognostic markers

Laboratory results; data within the last 3 months were recorded. Patients without results in the hospital database were excluded. Cardiometabolic control (waist circumference, body mass index, fasting blood glucose, HbA1C, mean arterial pressure and triglyceride) and GGT level were evaluated. HALP, PNI and NRI scores were calculated using haematological and biochemical values (Figure 1). The predictive and prognostic value of these tests in predicting the development of retinopathy in type 2 DM was evaluated.

Eye examinations and retinopathy evaluations

Visual acuity according to Snellen-chart, intraocular pressures with Goldmann applanation tonometry and fundus examination with indirect ophthalmoscope were performed by the same physician. Fundus examinations were performed with Goldman's three-mirror and Quadrospheric (Volk) contact lenses in patients who were deemed necessary by the clinician. Retinopathy staging was performed using the ınternational clinical classification system for diabetic retinopathy (Hoskins Center for Quality Eye Care) [23]. The control group without DR and the patient group consisted of patients with DR. The two groups were compared between clinical and demographic characteristics.

HALP: haemogram (g/L) x Albumin (g/L) x Lymphocyte/Thrombocyte

NRI: 14.87 x albumin (g/L) + 41.7 x weight/ideal weight (kg)
Ideal body weight calculation: 22 x height squared (m)

PNI: Albumin (g/L) + 5 *Lymphocyte (109/L)

Figure 1. Calculation of PNI, NRI and HALP score
HALP score: Haemoglobin, albumin, lymphocyte and platelet ratio, NRI: Nutritional risk index, PNI: Prognostic Nutritional Index

Markers of malnutrition

HALP, PNI and NRI scores calculated using laboratory values within three months were recorded for each patient during routine controls. The cut-off values of these values were found by ROC analysis and their predictive value in predicting the development of DR was calculated.

Statistical analysis

IBM SPSS Statistics for Windows was used for statistical analyses (Version 25.0" (IBM Corp., Armonk/NY/USA). Descriptive statistical methods (mean, SD, median, frequencies, ratios, min, max), the Student t test was used for two-group comparisons of normally distributed parameters and the Mann-Whitney U test for two-group comparisons of non-normally distributed parameters. Pearson and Spearman correlation analysis were used to assess relationships between parameters. Receiver operating characteristic (ROC) analysis was used. The study data were analysed using Kolmogorov-Smirnov normality assumption. Independent t-test and ANOVA test, which are parametric tests, were performed to determine whether there were significant differences between DR and DR stage groups with different variables. To compare categorical variables, the chi-squared test and Fisher's exact test were used. Significance was accepted at $p<0.05$.

Results

Of the 166 patients included in this study, 91 were female (55%) and 75 were male (45%). The age range of the patients was 30 to 75. The average age was 61 years old. Ophthalmological examinations were performed by the same ophthalmologist and standardised. Patients were categorised as having retinopathy (n:108 patients; Proliferative retinopathy (PR): 53 and Nonproliferative retinopathy (NPR): 55) and non-retinopathy (n:58 patients). Clinical and demographic data were analysed. Median age ($p<0.001$), FBG ($p<0.001$), creatinine ($p=0.01$), HbA1c ($p<0.001$) and microalbuminuria ($p=0.01$) were higher in DR patients. In addition, no significant correlation was found between the presence of DR and cholesterol, LDL, triglyceride, HDL, ALT and AST levels ($p>0.05$) (Table 1).

Table 1. Association of clinical and demographic data of the patients with the development of retinopathy

		With retinopathy (n=108)	Without retinopathy (n=58)	*p*
Median age		62±7	57±9	<0.001
Hypertension n (%)		88 (78.5)	23 (21.5)	<0.001
Diabetes Mellitus treatment (n, %)	**Oral Antidiabetic**	71 (58.6)	50 (41.3)	0.005
	Insulin	80 (87.9)	11 (12.1)	<0.001
BMI (body mass index) (kg/m²)		31.2 (27.7-34.0)	29.3 (26.5-35.0)	0.38
Waist circumference (cm)	**Median**	104 (97-114)	96 (92-104)	0.002
	Female	107 (96-120)	98 (92-110)	0.03
	Male	102 (97-110)	94 (93-101)	0.009
Mean arterial pressure (MAP) (mmHg)		93 (87-100)	87 (83-97)	0.05
Fasting blood glucose (mg/dl)		202±76	158±76	<0.001
Triglyceride (mg/dl)		178±104	175±109	0.93
HDL cholesterol (mg/dl)		47±11	49±14	0.41
LDL cholesterol (mg/dl)		123±45	124±39	0.56
HbA1C		8.7±1.8	7.6±2.3	<0.001
Microalbuminuria		470±815	172±184	0.002

$p<0.05$ was considered statistically significant

Mean arterial pressure (p=0.01), fasting blood glucose (p=0.03), triglyceride (p=0.008), BMI (p=0.02) and HbA1c level (p=0.04) were found to increase statistically significantly as GGT level increased. All results support a statistically significant relationship between GGT and metabolic syndrome (Table 2).

The duration of type 2 DM and the development of DR were significantly related (Table 3) (p<0.001). It was found that the group without DR was mostly in the first 10 years, NPR was more common in >10 years and PR was more common in >15 years (p<0.001) (Table 3 and Table 4). The predictive power of HALP, PNI and NRI scores, which are defined as malnutrition markers in the literature, in predicting DR was calculated (Figure 1). A significant correlation was not found between HALP, PNI and NRI levels and DR development and stage (p>0.05) (Table 4).

Table 2. The relationship of GGT interval values to cardiometabolic parameters

	GGT <19 (n:73)	GGT: 19-36 (n:68)	GTT >36 (n:25)	*p*
BMI (body mass index) (kg/m²)	31 (±5)	30 (±5)	33 (±5)	**0.02**
Waist circumference	103.4 (±11.9)	101.5 (±13.1)	109.1 (±4.5)	0.06
Mean Arterial Pressure (mmHg)	88 (±10)	92 (±9)	94 (±9)	**0.01**
Fasting blood glucose (FBG) (mg/dl)	74 (±70)	188 (±86)	220 (±75)	**0.03**
Triglyceride (mg/dl)	152 (±99)	188 (±107)	204 (±111)	**0.008**
LDL cholesterol (mg/dl)	119 (±139)	125 (±41)	135 (±56)	0.59
HbA1C	8.1 (±1.83)	8.31 (±2.18)	9.20 (±2.01)	**0.04**

p<0.05 was considered statistically significant

Table 3. Duration of diabetes and diabetic retinopathy

Diabetes Mellitus duration	With retinopathy (n=108)	Without retinopathy (n=58)	*p*
0-5 year, n (%)	8 (22.2)	28 (77.8)	<0.001
5-10 year, n (%)	12 (36.4)	21 (63.6)	<0.001
10-15 year, n (%)	26 (86.7)	4 (13.3)	<0.001
15-20 year, n (%)	18 (81.8)	4 (18.2)	<0.001
>20 year, n (%)	44 (97.8)	1 (2.2)	<0.001

p<0.05 was considered statistically significant

Table 4. Comparison of diabetic retinopathy stage and malnutrition markers

	Stages of diabetic retinopathy			
Duration of Diabetes Mellitus, n (%)	**No Diabetic Retinopathy (n=58)**	**Non-proliferative retinopathy (n=55)**	**Proliferative retinopathy (n=58)**	*p*
0-10	49 (84.5)	14 (25.5)	5 (9.4)	
10-20	8 (13.8)	24 (43.6)	21 (39.6)	<0.001
>20	1 (1.7)	17 (30.9)	27 (50.0)	
HALP, Mean±SD	2.15±2.73	1.9±0.69	1.64±0.44	0.277
NRI, Mean±SD	65.83±6.1	65.36±4.95	64±5	0.187
PNI, Mean±SD	41.07±8.74	42.6±6.76	42.19±7.52	0.553

HALP: hemoglobin + albumin + lymphocyte + platelet, NRI: nutritional risk index, PNI: prognostic nutritional index
P<0.05 was considered statistically significant

Discussion

In this study, we investigated the predictive value of cardiometabolic control, GGT levels and malnutrition in the prediction of the development of DR in patients with type 2 DM using current data from the literature. Cardiometabolic control (waist circumference, BMI, fasting blood glucose, HbA1C, mean arterial pressure and triglycerides) was evaluated with metabolic syndrome parameters. PNI, NRI and HALP score were calculated as prognostic markers to predict malnutrition. Median age, FBG, creatinine, HbA1c and microalbuminuria were higher in patients with DR. In addition, significant correlation was not found with cholesterol, LDL, triglyceride and HDL levels. MAP, FBG, triglyceride, BMI and HbA1c levels were found to increase significantly as GGT level increased. All results support a statistically significant relationship between GGT and metabolic syndrome. A significant relationship was found between the development of DR and the duration of type 2 DM. It was observed that the group without DR was mostly in the first 10 years, and DR development increased after the tenth year despite the presence of controlled diabetes. No significant correlation was found between DR and HALP, PNI, NRS (p>0.05).

Visual loss due to DR is thought to be caused by macular edema, tractional retinal detachment or neovascular glaucoma. Ischemia and neovascularisation occur in the tissue following impaired vascular permeability and microthrombi. A major role in the pathogenesis is played by biochemical (protein kinase C, glycation and polyol pathways) and angiogenesis-inducing factors such as vascular endothelial growth factor (VEGF) and insulin-like growth factor 1 (IGF-1). Patients are a heterogeneous group with different levels of retinopathy findings. Genetic susceptibility is also very important. Some patients develop minimal retinopathy despite a long period of hyperglycaemic disease and some patients have severe retinopathy despite regular glycaemic control. Genetic susceptibility can be mentioned in these patients [12, 24-27].

In the study conducted by Ren et al. [28] although many causes are blamed for the pathogenesis of DR, research is ongoing. It was emphasised that laboratory parameters measured with patient blood are the primary biomarker of DR. Many studies have been conducted considering that the detection of metabolites passing into the circulation through the impaired blood-retinal barrier due to the pathophysiological process may be diagnostic. The most common proteins have been studied and the only significant correlation was found with HbA1c. In this study, a positive correlation has been found between a number of proteins (FABP4, iNOS, homocysteine, PTX3, ADAM, ANGPTL3, TIMP, MMP) that predict inflammation and increased angiogenesis and DR. However, the availability of these tests in daily practice is limited. There are no detailed clinical studies including prognostic markers that are routinely evaluated by clinicians at each visit, calculated by haemogram and biochemical parameters and predict inflammation.

In studies involving diabetic chronic complications, GGT levels at upper reference range significantly associated with metabolic syndrome, cardiovascular disease, diabetic neuropathy and diabetic nephropathy (p<0.05) [29-33]. In this study, mean arterial pressure (p=0.01), fasting blood glucose (p=0.03), triglyceride (p=0.008), BMI (p=0.02) and HbA1c level (p=0.04) increased with increasing GGT level (19-36U/L) and were statistically significant. All results support a statistically significant relationship between GGT and metabolic syndrome (Table 2).

In patients with uncontrolled diabetes, chronic hyperglycaemia and high mean blood pressure impair autoregulation in retinal blood vessels. Leukocytes adhere to the vascular endothelium. As a result, endothelial integrity is impaired and vascular permeability increases. Neovascularisation is triggered due to retinal ischaemia. Its reflection in the laboratory is an increase in inflammation markers such as platelets, leukocytes and neutrophils [18]. Hyperglycaemia disrupts retinal blood flow by affecting metabolism at cellular level. Neovascularisation related proliferative changes. Increased VEGF and IGF1 trigger the pathogenesis leading to more advanced retinal disease. In this process, the presence of independent metabolic variables such as hypertension accelerates the pathogenesis [19].

In the study conducted by Perais et al. [34] 6391 studies were reviewed and data from 59 studies (35 were prospective cohort studies and

22 were retrospective studies) were included. Nineteen of the studies included type 2 DM. The number of participants was min: 100, max: 71817 and follow-up periods ranged from 1-20 years. Duration of diabetes, diagnosis at an early age, blood pressure, LDL, total cholesterol, HDL, triglycerides, HbA1c, BMI, gender, smoking/alcohol use and socioeconomic status were found to be predictive and prognostic for the development of DR. In addition, in a systematic review analysing data from 19 clinical trials, duration of diabetes, dyslipidaemia, poor glycaemic control, microalbuminuria and hypertension were risk factors for DR. In this study, FBG (p<0.001), creatinine (p=0.01), HbA1c (p<0.001) and microalbuminuria (p=0.01) were found higher in DR patients. In addition, no significant correlation was found with GGT (p=0.16), cholesterol (p=0.63), LDL (p=0.56), triglyceride (p=0.93), HDL (p=0.41), ALT (p=0.81) and AST (p=0.69) levels (Table 1).

In patients trying to live with a chronic disease, good glycaemic control certainly reduces microvascular complications. However, recommending a more aggressive diet by keeping the HbA1c target below 6.5 leads away from being protective from increasing risk of hypoglycaemia and malnutrition. Malnutrition and hypoglycaemia will increase the frequency of microvascular and macrovascular complications [20-22]. The predictive power of HALP, PNI and NRS score, which are defined as malnutrition markers in clinical studies in the literature, in predicting DR was calculated. No statistically significant correlation was found between HALP, PNI and NRI levels and DR development and stage (p>0.05) (Table 4). There was a feeling that prospective studies with larger numbers of patients might have been of value.

In the study conducted by Saini et al. [35] 57 patients with DR were included. A significant correlation was found between DR severity and diabetic nephropathy severity (p<0.05). Consistent with the literature, creatinine elevation (p=0.01) and positive microalbuminuria (p=0.01) was higher in DR patients. The presence of an accompanying chronic complication in patients with DM indicates a high likelihood of other complications. Patients should be informed about chronic complications and measures should be taken for early diagnosis and primary prevention.

In a prospective study of 7458 non-diabetic men with an average follow-up of 12.8 years, 194 men developed type 2 DM. Compared with the rest of the cohort, the levels of GGT were higher in the patients who went on to develop type 2 DM (15.3U/l; 20.9U/l; p<0.0001). In this study by Perry et al. [30] it was emphasised that high GGT level may be a simple marker of increased visceral adipose tissue and hepatic insulin resistance. In this study, GGT was high in all patients with no statistically significant difference between the two groups.

In the prospective study showing that diabetes duration is the strongest indicator of DR prevalence, 627 patients with DM followed for 8-10 years on average. Despite routine follow-up, 39% (n:247) of patients developed DR (1.8% proliferative retinopathy (PR), 36.2% nonproliferative retinopathy (NPR)). Patients without DR had a diabetes duration of less than ten years, which is consistent with our study. Increased BMI, elevated HbA1c and poor glycaemic control have been defined as additional risk factors in patients with DR. In this study, in the absence of additional risk factors, DR was less common in the first decade, whereas NPR and PR developed after the tenth year. Based on all these data, to prevent the development of type 2 DR, close monitoring of patients should ensure glycaemic control, HbA1c within target range, blood pressure control and metabolic control [6].

Zheng et al. [13] took data from the National Health and Nutrition Examination Survey database. 657 patients with a history of cardiovascular disease (CVD) from 2003 to 2018 included. The HALP score (haemoglobin, albumin, lymphocyte and platelet), which includes malnutrition, inflammation and anaemia, shown to predict CVD prognosis. Mortality of all causes were higher in low-HALP patients (p<0.05). In the literature, it was shown to be predictive in the prognosis of malignancy, cerebrovascular disease and heart failure [14-16]. To our knowledge, there is no clinical study in the literature showing the prognostic value of HALP in DR patients. HALP score allows simultaneous assessment of anaemia, malnutrition and inflammation. In this study, the predictive and prognostic relationship between HALP score and DR was evaluated. It was observed that HALP score level decreased when

DR developed, but no significant relationship was found (p=0.277).

Kurtul et al. [7] prognostic nutritional index (PNI) was applied to 128 consecutively recruited patients with type 2 DM. PNI levels of patients without DR significantly higher than with DR (44.49±3.10 and 41.20±4.81; p<0.001). The prevalence of insulin use (63.6% (n:28); 26.2% (n:22); p<0.001) and hypertension (59.1% (n:26); 40.5% (n:34); p=0.045) were higher in patients with DR. Low haemoglobin (12.8±1.8; 13.6±1.6; p=0.009) and low albumin levels (4.11±0.48; 4.44±0.31; p<0.001) were found in DR patients. This result supports the pathogenesis of DR initiated by hypoxia. When multivariate analysis was performed with these significant results, PNI (HR=0.845, 95% CI=0.735-0.971; p=0.017), duration of diabetes (HR=1.135, 95% CI=1.051-1.226; p=0.001) and creatinine (HR=8.468, 95% CI=1.773-40.454, p=0.007) were identified as independent and significant prognostic factors for DR [7]. It can be concluded that inflammation and malnutrition have an important role in causing DR [7, 24].

In the study conducted by Wei et al. [17] 612 type 2 DM patients were included. In patients with DR, malnutrition was found to be common. In order to prevent the development and progression of DR, it was interpreted that malnutrition should be avoided. PNI and NRI scores were used to assess malnutrition. Multivariate analysis showed that the incidence of DR was lower with higher PNI (HR=0.96,95% CI=0.92-1.00; p=0.033) and NRI (HR=0.95,95% CI=0.92-0.99; p=0.007). In this study and in the literature, significant results were obtained with both nutritional scores. Patients with malnutrition had higher mean age and lower BMI, haemoglobin, albumin and lymphocyte levels than patients without malnutrition.

In this study, it was found that diabetes duration, age, FBG, creatinine, HbA1c, microalbuminuria, mean arterial pressure, triglyceride, GGT level and cardiometabolic parameters evaluated together would be predictive for the prognosis of DR in type 2 DM patients. Although statistically significant data could not be obtained with malnutrition markers, we should avoid malnutrition while recommending a diabetic diet. We may unintentionally increase the incidence of DR while trying to control blood glucose. This study had some limitations that may have influenced the results;

(1) Receipt of single centre data,

(2) Relatively small sample size

(3) Lack of a healthy control group (healthy control group was not included because it was considered unethical to perform fundus examination in healthy volunteers without DM when they were asymptomatic)

(4) Since it was a cross-sectional study, causality was not evaluated and subsequent follow-up was not recorded. Similar limitations were present in the studies on DR in the literature.

In conclusion, annual detailed ophthalmological examination should be recommended in patients with type 2 DM. It should be kept in mind that patients may be asymptomatic until irreversible changes occur. The importance of this should be explained in diabetic patient education. Thus, it is thought that this complication that may lead to blindness can be prevented. When additional risk factors were analysed in patients with retinopathy, it was found that diabetes duration, poor glycaemic control, high HbA1c level and increased BMI were important risk factors for DR. Many risk factors for cardiovascular disease, metabolic syndrome and microvascular complications are associated with increased GGT activity at the upper levels of the reference range. Strict glycaemic control, lowering of HbA1c levels and lowering of blood pressure should be known to prevent the development and progression of DR. Proteinuria, elevated urea and creatinine levels were found in patients with DR. The presence of microalbuminuria is a harbinger of imminent development of retinopathy. Statistically significant correlation wasn't found between HALP, PNI and NRS levels, which are defined as malnutrition markers in the literature, and the development and stage of DR. It was thought that studies with a larger number of patients may be guiding. The importance of early diagnosis and treatment as well as primary prevention for diabetic microvascular complications is emphasised. Diabetic patients are susceptible to microvascular and macrovascular complications.

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Authors' contributions to the article

M.O. and M.U. constructed the main idea and hypothesis of the study. M.O. and Y.D. developed the theory and arranged/edited the material and method section. M.O., M.U. and Y.D. has done the evaluation of the data in the Results section. Discussion section of the article written by A.O., M.U., M.O., Y.D., A.A.A., O.A. and B.S. reviewed, corrected and approved. In addition, all authors discussed the entire study and approved the final version.