

Diabetic Retinopathy in Relation with eGDR Value in Patients with Type 1 Diabetes Mellitus

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Type 1 diabetes mellitus (T1DM) is a chronic disease which represents a major issue for public health. Type 1 diabetes is occurred most frequently in childhood and adolescence, although in recent years due to the increase in the prevalence of obesity in this category of population has been registered a growing number of cases of type 2 diabetes among children and adolescents (1, 2).

Keywords: *Type 1 diabetes mellitus, diabetic retinopathy, insulin resistance*

Type 1 diabetes mellitus (T1DM) is a chronic disease which represents a major issue for public health. Type 1 diabetes is occurred most frequently in childhood and adolescence, although in recent years due to the increase in the prevalence of obesity in this category of population has been registered a growing number of cases of type 2 diabetes among children and adolescents [1, 2].

As a result of the vascular complications, diabetes is the main cause of blindness, being responsible for up to 40% of the cases of kidney failure and is a determinant key of staff morbidity and mortality by cardiovascular cause [3-5].

Insulin resistance has been linked to the pathophysiology of type 2 diabetes mellitus (T2DM) and it has been proved to have an important role in the increase of the risk of cardiovascular complications [6-12]. It has been recently shown that insulin resistance plays an important role in the natural history of type 1 diabetes, although it is generally known that it is mainly due to immune destruction of the β -pancreatic cells [13-15].

Ginsberg has studied the association of insulin resistance with T1DM [16-17]. Subsequent studies [18-21] showed a

significant decrease in glucose disposal mediated by insulin among patients with T1DM suggesting the presence of insulin resistance. After a decade this combination has aroused the interest of many research studies [22-30] to investigate the possible mechanisms of insulin resistance in T1DM.

Experimental part

The aim of the study

The study aims are to determine the prevalence of diabetic retinopathy in Type 1 DM and to correlate it with the presence of risk factors (lifestyle, disease evolution status, onset of disease, metabolic control). Also, we tried to assess the degree of insulin resistance and its correlation with the occurrence of diabetic retinopathy.

Material and methods

The observational cross sectional survey was conducted over a three-year period 2010-2013. The timing of exploration of the patients under study consisted of a complete initial assessment of inclusion in the study group.

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The analysed group consisted of 200 subjects with type 1 DM. Patients with DM were recruited unselected from patients who underwent consultations in the specialized ambulatory, met the inclusion and exclusion criteria and signed informed consent. After the data collection, the database was created with EXCEL program.

We recorded demographic data (age, gender), anthropometric data (weight, height, body mass index, waist circumference, hip circumference), personal physiological history (menarhas, births, abortions, fetal macrosomia, menopause), personal pathological history (DM, hypertension, dyslipidaemia, stroke, myocardial infarction, obesity, autoimmune diseases, microvascular complications of DM (retinopathy, diabetic neuropathy, diabetic nephropathy)). Patients were questioned about smoking status.

The following laboratory blood counts were performed: serum creatinine, total cholesterol, HDL-cholesterol, triglycerides, uric acid, serum hemoglobin; LDL-cholesterol was calculated with Friedwald formula.

Diagnosis of diabetic retinopathy was determined by ophthalmological examination and eye photography.

Insulin resistance was estimated for type 1 DM by eGDR using the following formula: $eGDR = 24.31 - (12.22 \times AC / WC) - (3.29 \times Hypertension) - (0.57 \times A1c)$ where Hypertension - yes = 1, no = 0. Subjects with $eGDR \leq 7.5$ mg / kg / min were considered to have insulin resistance [31].

Recorded data were analyzed using the SPSS software 17:00 (IBM Corporation, Armonk, NY, USA). The methods used were: t-test, Mann-Whitney test, Chi-square test, simple binary logistic regression, multiparametric logistic regression, multiparametric logistic regression with stepwise covariate selection.

Results and discussions

We conducted a study of 200 subjects with type 1 DM (116 males and 84 females). The age at onset of diabetes was on average 21.49 years. The evolution of DM in the studied population was on average 16.21 years (fig. 1). A total of 6 patients (3%) had a DM duration of over 40 years.

Metabolic control was evaluated by the glycated hemoglobin (HbA1c), with an average of 8.4% (fig. 2).

Diabetic retinopathy (any stage) occurred in 53%, proliferative diabetic retinopathy was met in 61 patients, representing 30.5% (fig. 3, fig. 4).

We have statistically analysed the proliferative stage of diabetic retinopathy and there have been statistically

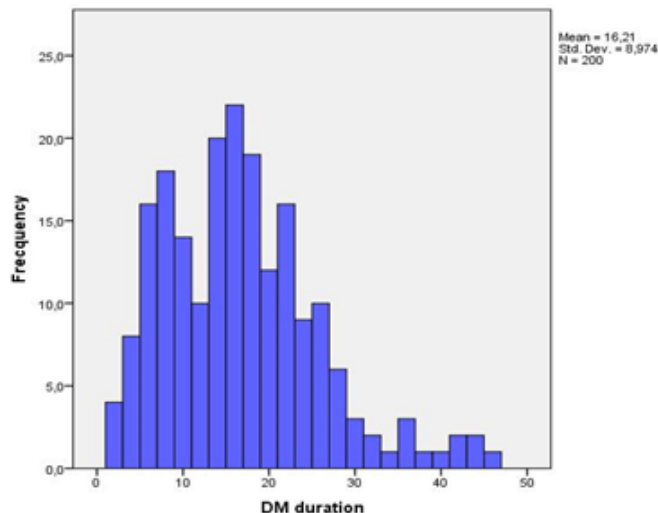


Fig. 1. Distribution of patients after the duration of DM evolution

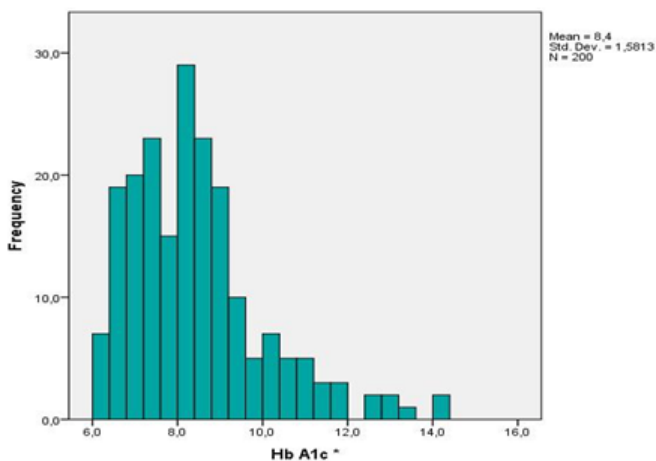


Fig. 2. Metabolic control evaluated by HbA1c value

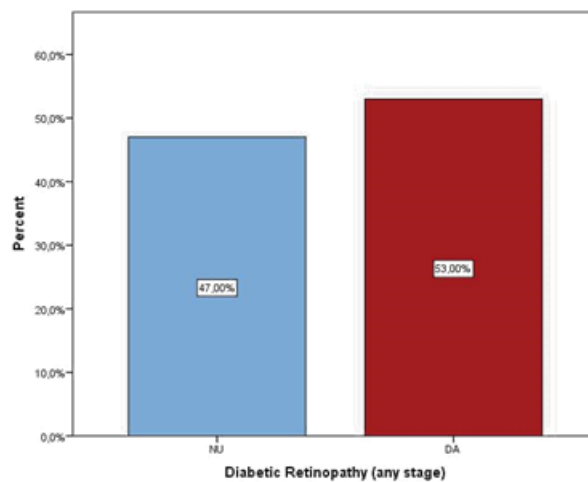


Fig. 3. Graphical representation of diabetic retinopathy (any stage)

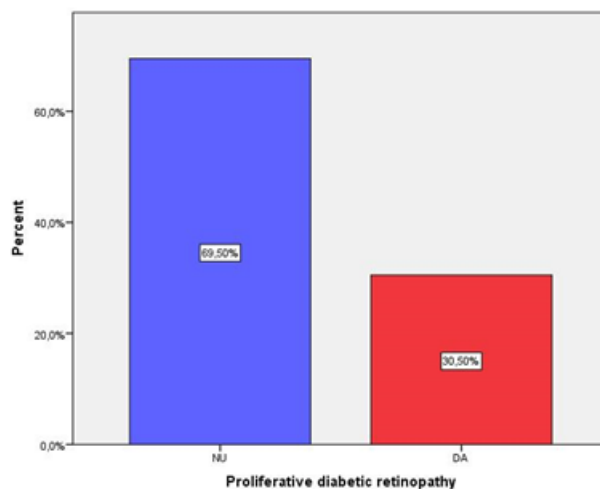


Fig. 4. Graphical representation of proliferative diabetic retinopathy

significant differences between patients with proliferative diabetic retinopathy and those without proliferative retinopathy in terms of age, duration of diabetes, eGDR, presence of hypertension, dyslipidemia and of hyperuricemia (table 1).

The mean age of patients with proliferative diabetic retinopathy and the duration of progression of diabetes is higher than those without proliferative diabetic retinopathy, the difference between the two groups being very statistically significant ($p < 0.001$).

Hypertension and hyperuricemia are present in more than half of the patients with proliferative diabetic retinopathy (49.1% and 56.7% vs. 48.9% and 43.1%, p

Variables	With proliferative diabetic retinopathy	Without proliferative diabetic retinopathy	p
Number of patients	61 (30.5%)	139 (69.5%)	N/A
Age (Years)	45.13±10.374	34.24±11.84	p< 0.001
Gender (M/W)	40/21	76/63	p=0.151
Duration of DM (years)	21.67±6.67	13.8±8.82	p< 0.001
BMI (Kg/m ²)	24.20±3.45	23.68±3.83	p=0.310
AC (cm)	89.26±10.38	88.07±10.15	p=0.529
HbA1c (%)	8.69±1.77	8.27±1.47	p=0.069
eGDR (mg·kg ⁻¹ ·min ⁻¹)	6.41±3.61	11.66±5.51	p< 0.001
Dyslipidemia	29 (47.5%)	71 (51%)	p< 0.001
Hypertension	30 (49.1%)	68 (48.9%)	p< 0.001
Hiperuricemia	34 (55.7%)	60 (43.1%)	p< 0.001

Table 1
CHARACTERISTICS OF PATIENTS WITH PROLIFERATIVE DIABETIC RETINOPATHY

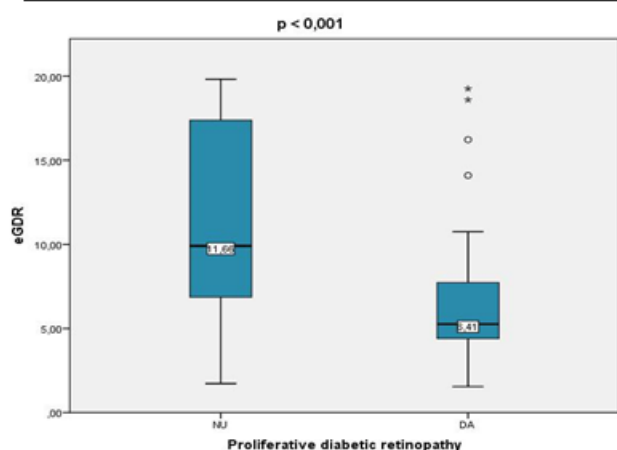


Fig. 5. Insulin resistance in patients with diabetic retinopathy

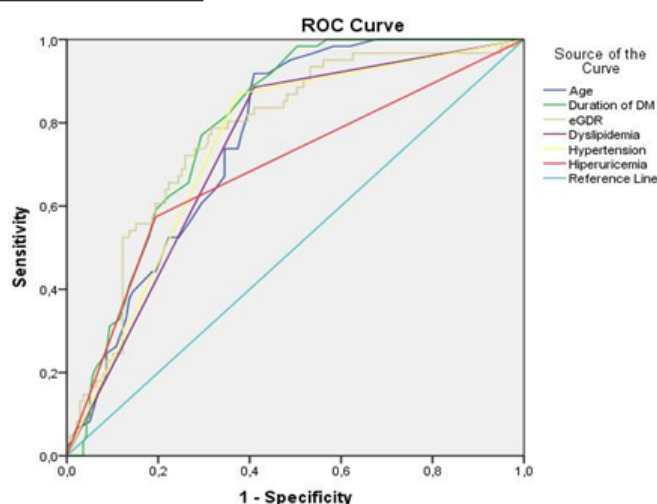


Fig. 6. Area under the ROC curve analysis for eGDR in patients with proliferative diabetic retinopathy

Variables	OR	95% CI	p
Age	1.080	1.049 – 1.111	p< 0.001
Duration of DM	1.114	1.068 – 1.161	p< 0.001
eGDR	0.793	0.729 – 0.863	p< 0.001
Dyslipidemia	11.098	4.711 – 26.143	p< 0.001
Hypertension	11.084	4.887 – 25.140	p< 0.001
Hiperuricemia	5.584	2.889 – 10.792	p< 0.001

Table 2
FINAL MODEL OF LOGISTIC REGRESSION FOR PROLIFERATIVE DIABETIC RETINOPATHY

Variables	Area under the ROC curve	95% CI
Duration of DM	0.797	0.737 – 0.857
Egdr	0.774	0.705 – 0.843
Age	0.763	0.699 – 0.827
Hypertension	0.747	0.677 – 0.818
Dyslipidemia	0.738	0.667 – 0.809
Hiperuricemia	0.690	0.606 – 0.774

Table 3
ANALYSIS OF AREA UNDER THE ROC CURVE FOR STATISTICALLY SIGNIFICANT PARAMETERS ASSOCIATED WITH PROLIFERATIVE DIABETIC RETINOPATHY

<0.001), while for dyslipidemia the situation is vice versa in the sense that it is higher percentage in patients without diabetic retinopathy.

The HbA1c value is higher in patients with proliferative retinopathy consistent with literature data, but in our study the correlation with the occurrence and progression of retinopathy is statistically insignificant (8.69 ± 1.77 vs. 8.27 ± 1.47 , $p = 0.069$). This is not conclusive, however, as a determined value was analysed at a given time, with no more HbA1c values determined over the evolution of DM to perform the HbA1c mean of each patient.

The eGDR value (expressed in $\text{mg} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) is lower in patients with proliferative retinopathy than in those without this complication (6.41 vs. 11.66; $p < 0.001$), indicating that patients with proliferative retinopathy exhibit a greater insulin resistance than those without proliferative retinopathy.

By performing the stepwise logistic regression analysis in which all the statistically significant parameters in table 1 were entered, the final regression model shown in table 2 is obtained.

The analysis of the area under the ROC curve used to assess the usefulness of studying the parameters in table 2 as independent predictors for the occurrence of diabetic retinopathy in subjects with type 1 DM shows that duration of DM evolution, followed by eGDR, age, presence of hypertension and dyslipidemia are the best predictors (table 3 and fig. 6).

Conclusions

The results of this study have shown that insulin resistance, quantified by eGDR, is more common in patients with diabetic retinopathy than in those without this complication. In addition, it showed that a low value of eGDR (insulin resistance) is independent associated with the presence of chronic complications of DM.

Older age and a long evolution of DM are factors known and shown in numerous studies to be associated with the development and progression of chronic complications in diabetes, whereas this new concept of insulin resistance has appeared lately in type 1 DM and it has gained ground worldwide being accepted by doctors and researchers. Its association with the emergence of chronic vascular complications in particular triggered the development of several studies that try to explain the link between insulin resistance and type 1 DM [32]. This result is very interesting because the presence of insulin resistance is not universally accepted, although it can be a good indicator of all chronic complications independent of other risk factors.

The present study has shown that insulin resistance is associated with an increased risk of chronic complications, but due to the cross-sectional design of this study, the causal relationship can not be evaluated. However, the existence of this causal relationship and the benefit of the treatment of insulin resistance in T1DM are issues to be debated in the future.

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