

Original Article

Frequency of retinopathy in prediabetic patients: A retrospective one-center study

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Abstract

Prediabetes is a condition in which glucose levels are high but do not reach the diagnostic limits of diabetes. The development of diabetes in prediabetic patients has been reported as 70% in some studies. Description of prediabetes is very important, as early diagnosis can prevent conversion to diabetes and diabetes complications. A number of observational studies have shown that prediabetes is associated with the risk of microvascular disease. In this study, it was aimed to identify prediabetic patients who started retinopathy. Our study is a retrospective study and was designed according to the 2022 guideline of the Turkish Endocrine and Metabolism Society (TEMS). It included 244 patients in the study. The presence of retinopathy was detected by performing a fundus examination of patients diagnosed with prediabetes. Of the 244 patients included in the study, 195 were female, 49 were male; mean age was 51.95±10.47 years, mean Body Mass Index (BMI) was 31.03±5.15 kg/m² and mean HbA1c was 6.03%±0.17. Diabetic retinopathy was detected in 33 of 244 (13.5%) cases. The most common comorbidity detected in patients with diabetic retinopathy was hyperlipidemia. The frequency of hyperlipidemia was 54.55%, and the frequency of retinopathy-positive cases with hyperlipidemia was 35.55%, which was statistically significant (p=0.037). There was no significant difference in the coexistence of nephropathy and retinopathy. The rate of retinopathy detected in prediabetic patients was consistent with the literature (13.5%, p<0.05). When the study is designed prospectively, we can get fluent answers to our questions by determining the type and stage of retinopathy. If prediabetes is taken seriously in terms of both its transformation into diabetes and co-existing diseases, the expenses to be made in this regard will also be prevented.

Keywords: prediabetes, retinopathy, nephropathy, microvascular complications.

Introduction

The prominence of micro and macrovascular complications can be seen long before the symptoms of diabetes become apparent. Many patients had myocardial infarction and were later diagnosed with diabetes. This condition is very common in cardiovascular diseases [1]. For this reason, prediabetes has gained great importance and first came to the fore in 2003 [2]. The terms “Impaired fasting glucose (IFG)” and “impaired glucose tolerance (IGT)” were proposed to be defined as “intermediate disorders of glucose metabolism” in the World Health Organization (WHO) 2007 report.

The American Diabetes Association (ADA), on the other hand, named IFG and IGT as prediabetes in 2003 (2). However, there have been some changes in the IFG and IGT criteria over the years.

The expert committee set the threshold for IFG as 100 mg/dL in 2003 [3]. Previously, this value was 110 mg/dL. In 2004, the ADA accepted the value determined by the expert committee for the IFG as the lower limit [4]. Our country defines IFG and IGT according to the TEMS (Turkish Endocrinology and Metabolism Society) guidelines, created based on ADA and IDF guidelines. This guide also adopted the criteria of the ADA and the expert committee [5]. According to these



guidelines, the diagnosis of IFG was formed as a fasting glucose value of 100–125 mg/dL and the diagnosis of IGT as 140–199 mg/dL 2nd-hour postprandial glucose or 2nd-hour glucose in the oral glucose tolerance test (OGTT) [5]. The prevalence of prediabetes is increasing all over the world. It is estimated that more than 470 million people will have prediabetes by 2030 [6]. Diagnosis and treatment of prediabetes are very important because this condition is associated with the risk of organ damage and death. The economies of the countries are also seriously affected. Some studies have disproved the idea of having fewer complications in prediabetes. Retinopathy is a detectable complication in prediabetes [7, 8]. Determining this situation is important from two aspects. The first one is to detect the complications earlier and intervene without developing diabetes. The second one is to predict the patient whose prediabetes is unknown in this way.

In this study, we aimed to detect the frequency and association of prediabetes and retinopathy.

Material and methods

The study was done retrospectively on the patients approved to Istanbul, University of Health Sciences, Fatih Sultan Mehmet Education and Research Hospital, and Internal Medicine Department. The Ethical approval was obtained for the study from Istanbul, University of Health Sciences, Fatih Sultan Mehmet Education and Research Hospital Clinical Trials Ethical Committee (Approval form number: 2022/38/Chairperson: Prof. Dr. Ali Özdemir) on April 28, 2022. The study included patients over 18 who applied to the hospital at Fatih Sultan Mehmet Education and Research Hospital, Internal Medicine Polyclinic, between January 2021 and March 2022. The study was conducted by the principles of the Declaration of Helsinki and in compliance with all international and national laws and regulations. Pa-

tients gave their written informed consent before any study procedure was performed.

The inclusion criteria are:

- Over 18 age male and female patients;
- According to the Turkish Endocrinology and Metabolism Society (TEMS) 2022 Guideline, IFG patients with fasting glucose value of 100–125 mg/dL and IGT patients with 75 g OGTT and postprandial blood glucose 140–199 mg/dL, HbA1c 5.6–6.4%;
- Having total cholesterol, HDL, LDL, triglyceride, fasting glucose, 2nd-hour postprandial glucose, HbA1c, uric acid, BUN, creatinine, ALT, AST, ferritin, 24 hour microalbuminuria, thyroid function tests;
- Fundus examination results on files.
- Complete age, patient history, physical examination, BMI, medication of patient information on files.

The exclusion criteria are:

- Below 18 age;
- Iron deficiency anemia;
- Hemoglobinopathies;
- Acute blood loss;
- Some pathologies that cause hemolysis;
- Transfusion history;
- Pregnancy;
- Uremia;
- Hypertriglyceridemia;
- Alcohol addiction;
- Steroid and diuretic use;
- Antidiabetic drug use.

Statistical analysis

The SPSS program was used in our statistical calculations study. Minimum-maximum, mean, and standard deviation values were included in descriptive statistics. A categorical Chi-square test was used in the data.

Table 1: Demographic and laboratory characteristics of the patients.

	One-sample statistics			
	N	Mean	Std. deviation	Std. error mean
Age	244	51.9549	10.46855	.67018
Height	244	162.8525	8.17723	.52349
Weight	244	82.0451	13.42139	.85922
BMI	244	31.0285	5.14567	.32942
Alc	244	6.0257	.17274	.01106

Table 1: Continued.

	One-sample statistics			
	N	Mean	Std. deviation	Std. error mean
FBG	244	105.3721	13.48777	.86347
LDL	243	124.1535	37.82915	2.42674
Triglyceride	242	126.7050	41.24665	2.65143
Creatinin	242	.7505	.13688	.00880
PPG	239	124.9862	23.59012	1.52592

Note: FBG – Fasting blood glucose; PPG – Postprandial glucose.

Table 2: Fundus involvement and HbA1c and PPG (postprandial glucose) relationship.

	Ranks			
	FUNDUS	N	Mean rank	Sum of ranks
HbA1c	0	209	119,30	24933,00
	1	35	141,63	4957,00
	Total	244		
PPG	0	209	118,65	24797,00
	1	35	145,51	5093,00
	Total	244		

Results

Two hundred and forty-four patients are included in the study. 195 of 244 patients were female, and 49 were male. The average age is 51.95 ± 10.47 years, mean BMI is 31.03 ± 5.15 kg/m², mean A1c is $6.03 \pm 0.17\%$ (Table 1).

Diabetic retinopathy (DRP) is detected in 33% of the 244 patients (Table 2). The frequency is 13.5% ($p < 0.005$). Seventeen patients have proteinuria (7%).

As comorbid diseases, 69 (28.3%) had hypertension (HT), 93 (38.1%) had hyperlipidemia, 7 (2.8%) had cor-

onary artery disease, 48 (19.7%) had hypothyroidism, 3 (1%) had hyperthyroidism.

There is no significant difference between the ages (52.79 ± 11.30 vs. 51.82 ± 10.35 years, $p = 0.624$), BMI (31.5 ± 5.39 vs. 30.96 ± 5.12 kg/m², $p = 0.574$) and A1c ($6.06 \pm 0.19\%$ vs. 6.02 ± 0.17 , $p = 0.254$) of those with and without retinopathy. The relationship between age and retinopathy is found, but the p-value is 0.488.

Retinopathy and postprandial glucose have a significantly different relationship ($p = 0.037$). However, the HbA1c and retinopathy relationship ($p = 0.088$) cannot

Table 3: Statistical analysis for PPG, HbA1c.

	Test statistics ^a	
	PPG	A1c
Mann-Whitney U	2852.000	3008.000
Wilcoxon W	24797.000	24953.000
Z	-2.086	-1.708
Asymp. Sig. (2-tailed)	.037	.088

Note: ^a – Grouping Variable: FUNDUS.

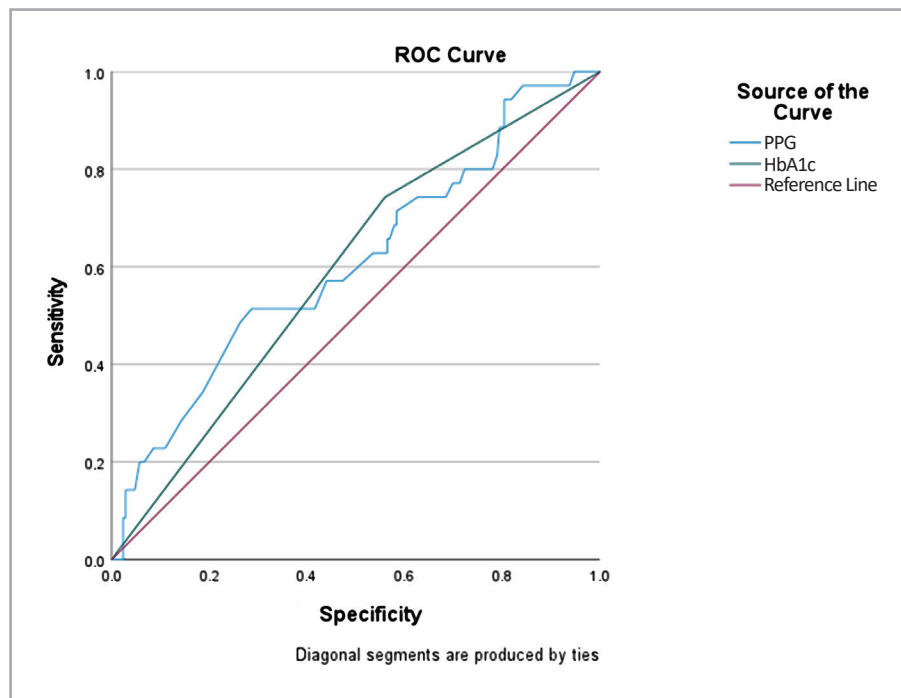


Figure 1: Diabetic retinopathy (DRP) sensitivity and specificity.

be mentioned (Table 3). As postprandial glucose and HbA1c levels increase, the sensitivity of DRP detection ratios is higher (Figure 1).

Considering the distribution of comorbid diseases in patients with DRP, the frequencies of HT and hypothyroidism are similar. Hyperlipidemia was detected more frequently in patients with DRP than in other comorbidities (54.55% vs. 35.55%, $p=0.037$).

However, there is no significant difference in the frequency of nephropathy between patients with and without DRP.

Discussion

Diabetes is considered one of the most important causes of blindness worldwide. In the long term, diabetes causes eye health problems such as cataracts, glaucoma, changes in visual acuity, and diabetic retinopathy (DR). Guliter *et al.* found that retinopathy was found in 18.8% of newly diagnosed patients with type 2 DM after ophthalmologic examination [9].

Taş *et al.* found retinopathy at a rate of 30.5% in the fundoscopic examination of 2362 diabetic patients [10]. In another study, the frequency of DR was found to be over 50% in the diabetic population [11].

Retinal vascular changes can also be seen during prediabetes [7, 12, 13]. Data on this subject are quite limited. DR was observed in 7.9% of patients with IGT and

12.6% of diabetic patients in the DPP study [14]. In a meta-analysis of 12 studies evaluating the data of 44623 patients, the prevalence of RP was found to be 0.1% in patients with IGT [15]. Contrary to the prevalence values found in the meta-analysis, the prevalence elevated to 12% in people with IGT in a study with Pima Indians [16]. This study was done in 991 patients with type 2 diabetes and 68 patients with IGT. In the Western Samoa Study, the prevalence of RT in IGT patients was found to be 10% [17].

In our study, the prevalence of DR was found to be 13.5%, which was significant. The other interesting issue in our study is that we detected a relationship between postprandial glucose and DRP but did not detect it at high HbA1c. Also, aging can make retinopathy risk easier, but there is no significant relationship between age and DRP. These findings are valuable for our thesis.

Our patients underwent an ophthalmological examination. However, an instrument such as optical coherence tomography angiography (OCTA) can also be used in such patients [18]. This method can detect higher prevalence.

On the other hand, there was no significant difference in the frequency of nephropathy in patients with and without retinopathy in our study. In a meta-analysis, the relationship between nephropathy and retinopathy in prediabetic patients was significant [13].

Hyperlipidemia is the most common disease co-existing with retinopathy in prediabetics in our study.

In some studies, the coexistence of hypertension was observed more frequently [19]. The high prevalence of retinopathy in our study may be related to ethnicity.

Our study's limitations include the fact that prediabetic individuals do not differentiate between IFG and IGT and the degree of retinopathy is not clearly distinguished.

In this study, a significant relationship was found between hypothyroidism and retinopathy. A re-study with a larger number of patients can be designed to address this issue.

Conclusion

Retinopathy is an important cause of blindness. Therefore, detecting this condition before diabetes is important and will prevent blindness. Therefore, eye examinations of these patients can be made routine. On the other hand, an unknown prediabetes patient may be detected during an eye examination and sent for a detailed test about this situation.

Conflict of interest

The authors declare no conflict of interest.

References

1. The DECODE Study Group on behalf of the European Diabetes Epidemiology Group: Glucose tolerance and cardiovascular mortality, comparison of fasting and 2-hour diagnostic criteria. *Arch Intern Med* 2001; 161(3): 397-404.
2. Standards of medical care for patients with diabetes mellitus. *Diabetes Care* 2003; 26 Suppl 1: S33-50.
3. Genuth S, Alberti KG, Bennett P, Buse J, Defronzo R, Kahn R, et al. Follow-up report on the diagnosis of diabetes mellitus. *Diabetes Care* 2003; 26: 3160-7.
4. Standards of medical care in diabetes. *Diabetes Care* 2004; 27 Suppl 1: S15-35.
5. TEMS 2022 Diabetes Guidelines p 16
6. Tabak AG, Herder C, Rathmann W, Brunner EJ, Kivimaki M. Prediabetes: a high-risk state for diabetes development. *Lancet* 2012; 379: 2279-90.
7. Klein R, Barrett-Connor EL, Blunt BA, Wingard DL. Visual impairment and retinopathy in people with normal glucose tolerance, impaired glucose tolerance and newly diagnosed NIDDM. *Diabetes Care* 1991; 14: 914-8.
8. Karadeniz S, Kir N, Yilmaz MT, Ongor E, Dincag N, Basar D, Akarcay K, Satman I, Devrim AS. Alteration of visual function in impaired glucose tolerance. *Eur J Ophthalmol* 1996;6: 59-62.
9. Güliter S, Ergin A, Emir M, Bayraktar Z. Yeni tanı konmuş diabetes mellituslu hastalarda retinopati prevalansı. *Retina-Vitreus* 1999;7(3):203-7.
10. Taş A, Bayraktar MZ, Erdem Ü, Sobaci G, Durukan AH, Karagül S et al. Diyabetik hastalarda retinopati sıklığı ve risk faktörleri. *Gülhane Tıp Dergisi* 2005; 47(3): 164-74.
11. Atmaca LS, Batioğlu F, İdil A. Tip 2 diyabetes mellitusta diyabetik retinopati: 2318 olguda ilk analiz. *MN-Oftalmoloji Dergisi* 1997; 4(4): 219-21.
12. Aydın E, Altın C, Emre S, Ağildere M, Tekindal MA. Glukoz Metabolizma Bozukluklarında Subklinik Aterosklerozun Değerlendirilmesi. *Ege J of Med* 2018; 57(4): 185-190.
13. Gabir MM, Hanson RL, Dabelea D, Imperatore G, Roumain J, Bennett PH, Knowler WC. Plasma glucose and prediction of microvascular disease and mortality: evaluation of 1997 American Diabetes Association and World Health Organization criteria for diagnosis of diabetes. *Diabetes Care* 2000; 23: 1113-18.
14. Diabetes Prevention Program Research Group. The prevalence of retinopathy in impaired glucose tolerance and recent-onset diabetes in Diabetes Prevention Program. *Diabet Med* 2007;24:137-44.
15. Colaguri S, Lee CM, Wong TY, Balkau B, Shaw JE, Borch-Johnsen K. Glycemic thresholds for diabetes-specific retinopathy: implications for diagnostic criteria for diabetes. *Diabetes Care* 2011; 34:145-50.
16. Nagi DK, Pettitt DJ, Bennett PH, Klein R, Knowler WC. Diabetic retinopathy assessed by fundus photography in Pima Indians with impaired glucose tolerance and NIDDM. *Diabet Med.* 1997; 14: 449-56.
17. Collins VR, Dowse GK, Plehwe WE, Imo TT, Toelupe PM, Taylor HR, Zimmet PZ. High prevalence of diabetic retinopathy and nephropathy in Polinesians of Western Samoa. *Diabetes Care* 1995; 18(8): 1140-9.
18. Lee J, Rosen R. Optical coherence tomography angiography in diabetes. *Curr Diab Rep* 2016;16(12): 123.
19. Gülcan E, Özcura F, Aydın S, Erbilin E, Koral L. Prediyabetik bireylerde diyabetik retinopati sıklığı ve etkileyen faktörler. *Göz-tepe Tıp Dergisi* 2008; 23(4):122-5.