

## Hospital Prevalence of Retinopathy in Patients with Newly-Diagnosed Type 2 Diabetes

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### ABSTRACT

**Aims:** To determine the period prevalence of diabetic retinopathy (DR) and the associated factors in patients with newly-diagnosed Type 2 diabetes mellitus (T2DM).

**Subjects and Methods:** In this prospective study, all newly-diagnosed T2DM patients who attended the ophthalmology clinic at King Fahad Hospital of the University between January 2012 and January 2015, were examined for DR. After pupillary dilation, the ophthalmic fundus was examined by a retina consultant using slit-lamp indirect ophthalmoscopy. Risk factors such as gender, age, hypertension, nephropathy, the level of glycated hemoglobin (Hb), microalbuminuria, and hyperlipidemia were evaluated for possible association with DR at the time of diagnosis.

**Results:** The study included 112 newly-diagnosed T2DM patients. DR was present in seven patients (6.25%) with a mean age of  $53.4 \pm 6.4$  years, four of whom were females (57%). Nonproliferative DR was present in all patients with DR, two patients (28.6%) presented with bilateral clinically significant macular edema requiring laser photocoagulation treatment and intravitreal anti-vascular endothelial growth factor therapy. In the study cohort, elevated hemoglobin A1C levels (HbA1C) were detected in 55 patients (49.1%), microalbuminuria in 28 (25.0%), hypertension in 31 (27.6%), hyperlipidemia in 65 (58.0%) and obesity in 43 (38.1%). At the time of T2DM diagnosis, uncontrolled HbA1C levels were significantly associated with the presence of retinopathy ( $P = 0.045$ ); however, no statistical significance was observed for the remaining risk factors.

**Conclusion:** The frequency of retinopathy in newly-diagnosed T2DM patients was similar to previous reports. Vision-threatening maculopathy was present in two of seven patients, requiring further intervention. Therefore, early screening is strongly recommended for all newly-diagnosed T2DM patients. Prospective studies with a large sample size are needed to verify the risk factors for these patients.

**Key words:** Associated factors, newly-diagnosed Type 2 diabetes, prevalence, retinopathy

ملخص البحث:

تناقش هذه الدراسة المستقبلية مدى انتشار اعتلال الشبكية لدى مرضى السكري من النوع الثاني المشخصين حديثاً والتي أجريت في مستشفى الملك فهد الجامعي بالخبر. شملت الدراسة 112 مريضا فكانت اعتلال الشبكية أصابت 7 مرضى (6.25%) أما اعتلال الشبكية الخلفية فكانت موجودة لدى جميع المرضى. كما أظهرت الدراسة ارتفاعاً في مخزون السكر عند 55 مريضاً (49.1%) إضافة إلى بعض التنبؤات المصاحبة

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لمرض السكري. بينت هذه الدراسة تواتر اعتلال الشبكية لدى مرضى السكري من النوع الثاني حديثي التشخيص. ينصح الباحث بإجراء دراسات أخرى تحتوي على أعداد أكبر لتحديد العوامل الأخرى لاعتلال الشبكية وفحص لكل مرضى السكري من النوع الثاني حديثي التشخيص.

## INTRODUCTION

Diabetes mellitus is a major public health problem that is approaching epidemic proportions globally. Type 2 diabetes mellitus (T2DM) poses a major global health threat affecting both developed and developing countries.<sup>[1]</sup> The prevalence of T2DM worldwide has been estimated to have risen from 150 million to 225 million by the end of 2010 and expected to rise to 300 million by 2025.<sup>[2,3]</sup> Diabetic retinopathy (DR) is one of the most common and serious complications of diabetes and is a leading cause of blindness worldwide in adults aged 20–60 years.<sup>[4,5]</sup> The prevalence of retinopathy in newly-diagnosed T2DM patients ranges from 5 to 35%.<sup>[6]</sup> Blindness from DR can be delayed with timely detection and appropriate therapy.<sup>[7]</sup> In the Kingdom of Saudi Arabia (KSA), approximately 23.7% of the population (age 30–70 years) have T2DM.<sup>[8]</sup> Because of the high prevalence rates of T2DM in KSA, there is a need for baseline data regarding the prevalence of DR among newly diagnosed T2DM patients. Therefore, this study was carried-out to assess the hospital prevalence rates of DR and the associated risk factors for its presence among the newly-diagnosed T2DM patients.

## SUBJECTS AND METHODS

This prospective study was conducted at King Fahad Hospital of the University, Al-Khobar, Saudi Arabia, between January 2012 and January 2015. Newly-diagnosed T2DM patients were diagnosed using the World Health Organization (WHO) criteria and were defined as those patients presented within one month of their diagnosis.<sup>[9]</sup> Our study included a cohort of 112 patients who were enrolled sequentially.

Patients' age, gender, nationality, height, body weight, blood pressure, history of smoking and hypertension were recorded. Each patient underwent slit-lamp biomicroscopy examination by a retina consultant and color fundus photography of both eyes after pupillary dilatation with tropicamide 1%. If DR was present, the severity of retinopathy in each eye was determined for each patient according to standard protocol. The retinopathy was graded into nonproliferative DR (NPDR), NPDR with maculopathy, proliferative DR (PDR) and advanced PDR.<sup>[10]</sup>

Patients were assessed for the presence of other risk factors such as hyperglycemia, nephropathy, hypertension, hyperlipidemia, smoking and obesity. Glycemic control was evaluated by measuring glycated hemoglobin A1C (HbA1C) levels. Optimal glycemic control was defined as HbA1C <7%. To assess the presence of nephropathy, microalbuminuria levels were measured in first-voided early morning urine samples (normal values <19 mg/L). The urine test was repeated twice (2–4 weeks apart) and other causes for microalbuminuria were excluded. The systolic and diastolic blood pressures were recorded for all patients. According to the WHO criteria, hypertension was defined when supine systolic blood pressure exceeded 140 mm Hg, or diastolic blood pressure exceeded 90 mm Hg. Hyperlipidemia was determined from blood samples taken after a 12 h fast, according to the WHO criteria.<sup>[11]</sup> Hyperlipidemia was defined as elevated total cholesterol (>5.2 mmol/L), low-density lipoprotein (>4.5 mmol/L), or high triglyceride (>2.28 mmol/L), or low high-density lipoprotein (<1 mmol/L) levels.

Height was measured to the nearest 0.5 mm and weight to the nearest 0.1 kg. As recommended by the WHO, the standard classification of overweight and obesity was based on the body mass index (BMI), a BMI of 30 kg/m<sup>2</sup> or greater was considered as obesity.<sup>[12]</sup>

Patients with newly-diagnosed T2DM were divided into two categories: Absent or present DR. The role of risk factors in the presence of DR was evaluated by statistical analysis using the Chi-square test. Statistical analysis was performed using the Statistical Package for Social Sciences (version 20.0; SPSS Inc., Chicago, IL). *P* < 0.05 was considered statistically significant. The study was approved by the Institutional Review Board. Written informed consent was obtained from each subject prior to the study.

## RESULTS

The study sample included 112 patients (62 female and 50 male patients; mean age, 51.2 ± 5.3 years; 91 Saudi nationals and 21 expatriates; 19 current and former smokers). Uncontrolled HbA1C was identified in 55 patients (49.1%), microalbuminuria in 28 (25.0%), hypertension in 31 (27.6%), hyperlipidemia in 65 (58.0%) and obesity in 43 (38.1%).

DR was identified in both eyes in seven patients (6.25%; four female and three male patients; mean age,  $53.4 \pm 6.4$  years; all nonsmokers). All these patients presented with NPDR, and two of them had additional bilateral clinically significant macular edema. Evaluation of the macula with slit-lamp biomicroscopy and optical coherence tomography showed significant maculopathy in both cases. Patients were further treated with focal laser treatment in combination with anti-vascular growth endothelial factor intravitreal injections. Moreover, uncontrolled HbA1C levels were significantly associated with the presence of DR ( $P = 0.045$ ) at T2DM diagnosis. No statistically significant association was found for the other risk factors analyzed [Table 1].

## DISCUSSION

In our findings, the relatively low proportion of DR (6.25%) among newly-diagnosed T2DM patients is similar to that reported in studies from Kuwait (7.6%), Denmark (5%), Australia (6.2%) and Southern India (7.3%), but differs from that reported in studies from Romania (14.37%), Taiwan (25.5%) and the United Kingdom Prospective Diabetes Study (UKPDS) group in the United Kingdom (35%).<sup>[17,12-17]</sup> Although it is difficult to identify the reasons for such variation in prevalence rates among several populations, race, age, method of detecting DR, health care facilities and other risk factors could have contributed to the differences.

Some studies have shown that age at diagnosis of T2DM is a risk factor for the presence of DR, with the risk

increasing with age.<sup>[18-20]</sup> This observation is probably related to longer hyperglycemia periods at the time of diagnosis. In the current study, age (>51 years) was not a statistically significant risk factor ( $P = 0.403$ ) for DR. Furthermore, in contrast to the finding of Liu *et al.*, we and other researchers have reported that gender was not a significant factor for the presence of DR at T2DM diagnosis.<sup>[18,20]</sup>

HbA1C is the gold standard measurement for the assessment of glycemic control. Clinical trials demonstrated a 25% reduction in microvascular complications per 1% reduction in HbA1C levels.<sup>[21]</sup> In our study, six of the seven patients with DR presented high levels of HbA1C, showing a statistically significant correlation ( $P = 0.045$ ) between DR and HbA1C levels. These results are in agreement with those obtained by Nguyen *et al.* and Owens *et al.* who reported that an elevated HbA1C level is a risk factor for the presence of DR among newly diagnosed T2DM patients.<sup>[18,22]</sup> Similarly, van Leiden *et al.* showed that DR may be present in individuals with impaired glucose tolerance without a diagnosis of T2DM, thereby validating the hypothesis that T2DM and DR may be present for several years before clinical diagnosis.<sup>[23,24]</sup>

The other biochemical parameters analyzed have been reported to be positively associated with DR in newly-diagnosed T2DM patients (hyperlipidemia and microalbuminuria); however, as seen in the studies by Rema *et al.* and Nguyen *et al.*, our study showed no association between these risk factors and DR.<sup>[15,14,16,22,23,25,26]</sup> In fact, in our study, five of the seven patients with DR presented high lipid levels. Notably, albuminuria was present in three of the seven (57.1%) patients with DR compared to 25 of 105 (23.8%) patients without DR. Herein, we have described a trend ( $P = 0.259$ ) for increased albuminuria with increasing DR. In our study, the other risk factors analyzed (hypertension, BMI, and smoking) were not associated with DR; however, other studies have described hypertension or BMI as risk factors in T2DM patients with DR.<sup>[17,18,23]</sup> In agreement with our study, studies by Nguyen *et al.* and Owens *et al.* reported a negative association.<sup>[18,22]</sup> Notably, the UKPD study showed that the severity of DR increased in lean women compared to that in obese women.<sup>[17]</sup>

The effects of smoking on DR are unclear.<sup>[27]</sup> However, Eliasson reported that in Type 1 diabetic patients,

**Table 1: Risk factors studied for the presence of retinopathy in newly diagnosed type 2 diabetes mellitus**

Variable	DR present (n=7) (%)	DR absent (n=105) (%)	P
Age (>51 years)	5 (71.4)	58 (55.2)	0.403
Male	3 (42.9)	47 (44.8)	0.921
Female	4 (57.1)	58 (55.2)	
Smokers	0 (0)	19 (18.1)	0.216
Non-smokers	7 (100)	86 (81.9)	
High HbA1C	6 (85.7)	49 (46.7)	0.045
Hypertension	3 (42.9)	28 (26.7)	0.859
Hyperlipidemia	5 (71.4)	60 (57.1)	0.545
Microalbuminuria	3 (42.9)	25 (23.8)	0.259
Obesity	3 (42.9)	40 (38.1)	0.802

cigarette smoking increases the risk for DR, probably via its metabolic effects in combination with increased inflammation and endothelial dysfunction.<sup>[28]</sup>

Particularly noteworthy, in agreement with several studies by de Fine Olivarius *et al.*, vision-threatening maculopathy was present in two of the seven patients.<sup>[13]</sup> These cases indicate that some patients may already be in need of treatment for DR at the time of T2DM diagnosis. Thus, funduscopy examination of all newly-diagnosed T2DM patients is of paramount importance. The principal limitation of this study is the relatively small sample size. Hence, further studies with a larger sample size are needed and may reveal more statistically significant values. The identification of risk factors in newly diagnosed T2DM is essential for physicians to recognize a subset of patients who need to be further investigated for the presence of DR.

## CONCLUSION

The prevalence of DR in newly-diagnosed T2DM patients was relatively low, and only two patients presented vision-threatening maculopathy at T2DM diagnosis.

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## Conflicts of interest

There are no conflicts of interest.

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