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

Waseem M. AL-Zamil
Department of Ophthalmology, College of Medicine, University of Dammam, Dammam, Saudi Arabia

Correspondence: Dr. Waseem M. Al-Zamil, Department of Ophthalmology, University of Dammam, P.O. Box 2208, Al Khobar 31952, Saudi Arabia. E-mail: waseem_alzamil@hotmail.com

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 ± 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
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. 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. 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. The prevalence of retinopathy in newly-diagnosed T2DM patients ranges from 5 to 35%. Blindness from DR can be delayed with timely detection and appropriate therapy. In the Kingdom of Saudi Arabia (KSA), approximately 25.7% of the population (age 50–70 years) have T2DM. 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. 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.

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. 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/m² or greater was considered as obesity.

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 ± 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%). 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.[18-20] 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.[18,20]

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.[21] 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.[18,22] 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.[23,24]

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.[15,14,16,22,25,25,26] 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.[17,18,23] In agreement with our study, studies by Nguyen et al. and Owens et al. reported a negative association.[18,22] Notably, the UKPD study showed that the severity of DR increased in lean women compared to that in obese women.[17]

The effects of smoking on DR are unclear.[27] 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.\textsuperscript{[28]}

Particularly noteworthy, in agreement with several studies by de Fine Olivarius et al., vision-threatening maculopathy was present in two of the seven patients.\textsuperscript{[13]} These cases indicate that some patients may already be in need of treatment for DR at the time of T2DM diagnosis. Thus, funduscopic 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.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**REFERENCES**

1. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27:1047-53.
2. Zimmet P. The burden of type 2 diabetes: Are we doing enough? Diabetes Metab 2003;29(4 Pt 2):659-18.
3. Mainous AG 3\textsuperscript{rd}. Baker R, Koopman RJ, Saxena S, Diaz VA, Everett CJ, \textit{et al.} Impact of the population at risk of diabetes on projections of diabetes burden in the United States: An epidemic on the way. Diabetologia 2007;50:934-40.
4. Kalvodová B. Screening for diabetic retinopathy in the Czech Republic – Guideline. Česk Slov Oftalmol 2002;38:3-10.
5. Viswanath K, McGavin DD. Diabetic retinopathy: Clinical findings and management. Community Eye Health 2003;16:21-4.
6. Tapp RJ, Shaw JE, Harper CA, de Courten MP, Balkau B, McCarty D, \textit{et al.} The prevalence of and factors associated with diabetic retinopathy in the Australian population. Diabetes Care 2003;26:1731-7.
7. Aiello LP, Cahill MT, Wong JS. Systemic considerations in the management of diabetic retinopathy. Am J Ophthalmol 2001;132:760-76.
8. Al-Nozha MM, Al-Maatouq MA, Al-Mazrou YY, Al-Harthi SS, Arafah MR, Khalil MZ, \textit{et al.} Diabetes mellitus in Saudi Arabia. Saudi Med J 2004;25:1603-10.
9. Prevention of diabetes mellitus: Report of a WHO study group. World Health Organ Tech Rep Ser 1994;844:93.
10. Goldberg MF, Jampol LM. Knowledge of diabetic retinopathy before and 18 years after the Airlie house symposium on treatment of diabetic retinopathy. Ophthalmology 1987;94:741-6.
11. Lyznicki JM, Young DC, Riggs JA, Davis RM; Council on Scientific Affairs, American Medical Association. Obesity: Assessment and management in primary care. Am Fam Physician 2001;63:2185-96.
12. Al-Zuabi H, Al-Tammar Y, Al-Moataz R, Al-Sabti K, Wani VB, Hamama F, \textit{et al.} Retinopathy in newly diagnosed type 2 diabetes mellitus. Med Prin Pract 2005;14:293-6.
13. de Fine Olivarius N, Nielsen NV, Andreasen AH. Diabetic retinopathy in newly diagnosed middle-aged and elderly diabetic patients. Prevalence and interrelationship with microalbuminuria and triglycerides. Graefes Arch Exp Ophthalmol 2001;239:664-72.
14. Rema M, Deepa R, Mohan V. Prevalence of retinopathy at diagnosis among type 2 diabetic patients attending a diabetic centre in South India. Br J Ophthalmol 2000;84:1058-60.
15. Talu S, Kaucsar E, Soreanu A. Diabetic retinopathy in newly diagnosed patients with type II diabetes mellitus. Ophthalmologica 2002;54:27-30.
16. Tzeng TF, Hsiao PJ, Hsieh MC, Shin SJ. Association of nephropathy and retinopathy, blood pressure, age in newly diagnosed type 2 diabetes mellitus. Kaohsiung J Med Sci 2001;17:294-301.
17. Kohner EM, Aldington SJ, Stratton IM, Manley SE, Holman RR, Matthews DR, \textit{et al.} United Kingdom prospective diabetes study, 30: Diabetic retinopathy at diagnosis of non-insulin-dependent diabetes mellitus and associated risk factors. Arch Ophthalmol 1998;116:297-303.
18. Owens DR, Volund A, Jones D, Shannon AG, Jones IR, Birtwell AJ, \textit{et al.} Retinopathy in newly presenting non-insulin-dependent (type 2) diabetic patients. Diabetes Res 1988;9:59-65.
19. Wang WQ, Ip TP, Lam KS. Changing prevalence of retinopathy in newly diagnosed non-insulin dependent diabetes mellitus patients in Hong Kong. Diabetes Res Clin Pract 1998;39:185-91.
20. Liu DP, Molyneaux L, Chua E, Wang YZ, Wu CR, Jing H, \textit{et al.} Retinopathy in a Chinese population with type 2 diabetes: Factors affecting the presence of this complication at diagnosis of diabetes. Diabetes Res Clin Pract 2002;56:125-31.
21. Saadine JB, Engelgau MM, Beckles GL, Gregg EW, Thompson TJ, Narayan KM. A diabetes report card for the United States: Quality of care in the 1990s. Ann Intern Med 2002;136:565-74.
22. Nguyen HT, Luzio SD, Dolben J, West J, Beck L, Coates PA, \textit{et al.} Dominant risk factors for retinopathy at clinical diagnosis in patients with type II diabetes mellitus. J Diabetes Complications 1996;10:211-9.
23. van Leiden HA, Dekker JM, Moll AC, Nijpels G, Heine RJ, Bouter LM, \textit{et al.} Blood pressure, lipids, and obesity are associated with retinopathy: The hoorn study. Diabetes Care 2002;25:1320-5.
24. Harris MI, Klein R, Welborn TA, Knowin MW. Onset of NIDDM occurs at least 4-7 yr before clinical diagnosis. Diabetes Care 1992;15:815-9.
25. Manaviat MR, Afkhami M, Shoja MR. Retinopathy and
26. Gall MA, Rossing P, Skott P, Damsbo P, Vaag A, Bech K, et al. Prevalence of micro- and macroalbuminuria, arterial hypertension, retinopathy and large vessel disease in European type 2 (non-insulin-dependent) diabetic patients. Diabetologia 1991;34:655-61.

27. Jain A, Sarraf D, Fong D. Preventing diabetic retinopathy through control of systemic factors. Curr Opin Ophthalmol 2003;14:389-94.

28. Eliasson B. Cigarette smoking and diabetes. Prog Cardiovasc Dis 2003;45:405-13.