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Non-mydriatic fundus camera screening with diagnosis by telemedicine for diabetic retinopathy patients with type 1 and type 2 diabetes: a hospital-based cross-sectional study

Maram Yaslam,[a] Fadwa Al Adel,[b] Khalid Al-Rubeaan,[c] Rakan K. AlSalem,[c] Musab A. Alageel,[c] Abdaulaziz Alsalhi,[c] Dehkra AlNageeb,[d] Amira M. Youssef[e]

From the [a]College of Medicine, University Diabetes Center, King Saud University; [b]Department of Ophthalmology, College of Medicine, Princess Nourah bint Abdulrahman University, Riyadh, Saudi Arabia; [c]College of Medicine, King Saud University, Riyadh, Saudi Arabia; [d]Research Department, King Saud University, Riyadh, Saudi Arabia; [e]Registry Department, King Saud University, Riyadh, Saudi Arabia

Correspondence: Dr. Fadwa Al Adel, · Department of Ophthalmology, College of Medicine, Princess Nourah bint Abdulrahman University, PO Box 84428, Riyadh 11671, Saudi Arabia· +966-11-8238722 · ffaladel@pnu.edu.sa · ORCID: https://orcid.org/0000-0003-4516-380X

BACKGROUND: Diabetic retinopathy (DR) is considered the fifth leading cause of visual impairment worldwide and is associated with a huge social and economic burden.

OBJECTIVE: Describe the practicality of non-mydriatic funduscopic screening photography for the detection of DR among patients with type 1 and type 2 diabetes.

DESIGN: Cross-sectional hospital-based study.

SETTING: Diabetes center, Riyadh.

PATIENTS AND METHODS: Between July and December 2017, patients with diabetes and aged ≥18 years were selected by systematic random sampling from the University Diabetes Center. Fundoscopic eye examination was performed using the TRC-NW8 non-mydriatic camera, which performs ocular coherence tomography (OCT) to detect macular edema. Using telemedicine, pictures were graded by a retinal-specialized ophthalmologist using the international clinical DR disease severity scale. Patients were classified according to the type and severity of DR.

MAIN OUTCOME MEASURES: Detection and classification of DR.

SAMPLE SIZE: 978 Saudi patients with diabetes.

RESULTS: Of 426 (43.5%) patients with DR, 370 had nonproliferative DR and 55 had proliferative DR. Nineteen (1.9%) had macular edema. The most important risk factors for DR were longer diabetes duration and poor glycemic control. Both older age and insulin use contributed to the higher prevalence of DR and macular edema. DR was more common among type 1 patients at 55.4% compared with 49% among type 2 patients. In addition, more females had macular edema (57.1% versus 42.9% among males). Nine patients with macular edema (47.3%) had hypertension while 154 of 426 patients with DR (36.2%) had hypertension.

CONCLUSION: Non-mydriatic funduscopic screening photography was practical and useful for the detection of DR in patients with type 1 and type 2 diabetes.

LIMITATIONS: Conducted in a single center.

CONFLICT OF INTEREST: None.

Diabetic retinopathy (DR) is considered as the fifth leading cause of visual impairment worldwide and is associated with a huge social and economic burden on the healthcare system.[1] Considering the increasing prevalence of DR throughout the world, the World Health Organization (WHO) unit for the prevention of blindness defined different approaches for screening, early detection, and management in populations in various settings.[2] In 2012, the global prevalence of DR among patients with diabetes was estimated at 34.6%, where 6.96% was proliferative DR (PDR), 6.81% diabetic macular edema, and 10.2% vision-threatening DR.[3] Many studies have shown that screening programs are effective in reducing the progression of DR and the rate of blindness.[4,5] Therefore, initiation of screening programs is essential in detection of intraretinal microvascular abnormalities (IRMA) to reduce the rate of blindness among the diabetic community.

Screening for DR is conducted either by a direct ophthalmic examination or by mydriatic or non-mydriatic retinal photographic screening.[4] In several studies, direct ophthalmoscopy failed to meet the 80% sensitivity and specificity target.[6] In contrast, fundus examination following mydriasis has high sensitivity and specificity rates of 97% and 92%, respectively, compared to non-mydriatic fundus photography[7] with a sensitivity and specificity of 78% and 86%, respectively.[8]

The University Diabetes Center at King Saud University has a structured referral system for DR screening by well-trained ophthalmology nurses using a non-mydriatic camera for fundoscopic eye examinations that are read remotely by telecommunicating with ophthalmologists specialized in retinal diseases. The current study assessed the frequency of different forms of diabetic retinopathy in the study population of patients with type 1 and type 2 diabetes to highlight the practicality of this screening program. In addition, the screening program identified important risk factors for retinopathy in our community.

PATIENTS AND METHODS

To assess the DR screening program used at the University Diabetes Center at King Saud University in Riyadh, a cross-sectional cohort was selected using systematic random sampling. The initial patient selection was done through several steps including defining and listing the study population that was referred from the UDC to the ophthalmology clinic between July and December 2017. We then calculated the sample fraction that was 1/2 and selected the first patient using the random number table, which was the fifth patient in the patient list. We then selected every other patient

starting with the fifth patient. Patients were included in this study if they were ≥18 years of age regardless of their gender or diabetes type and duration. Patients were classified as having type 1 or type 2 diabetes per the American Diabetes Association criteria.[9] The patients were interviewed to collect demographic data, including age, gender, duration of diabetes, and history of hypertension. Patients were then classified according to their diabetes management and divided into three groups; patients managed with oral hypoglycemic agents, insulin, or both. Each subject's height and weight were measured, and a blood sample was collected for measurement of glycated hemoglobin (HbA1c) using the COBAS INTEGRA 400 analyzer (Roche Diagnostics, USA).

The process of funduscopic photography acquisition was explained to each patient. Patients with unclear images (due to media opacity such as a corneal scar, cataract, and vitreous hemorrhage) had their pupils dilated using 1% Mydriacyl (tropicamide). Otherwise, patients had their photos taken without pupil dilation. A well-trained ophthalmology nurse took the funduscopic images of both eyes using two fields only, namely, macula-centered and disc-centered, using non-mydriatic cameras 3D OCT-1 Maestro (optical coherence tomography) and TRC-NW8 (Topcon Corporation, Tokyo, Japan). These cameras acquire a macular ocular coherence tomography (OCT) image at the same time as the fundus image acquisition.

All funduscopic images were graded by retina specialists using the International Clinical Classification of Diabetic Retinopathy Disease severity scale.[10] Patients were considered free from retinopathy if there were no abnormalities. They were considered to have mild nonproliferative DR (NPDR) if they had microaneurysms only or moderate NPDR if they had more than just microaneurysms but not severe NPDR. Severe NPDR was considered if any of the following was observed with no signs of proliferative retinopathy: more than 20 intraretinal hemorrhages in each of four quadrants, definite venous beading in two or more quadrants, or prominent intraretinal microvascular abnormality in one or more quadrants. PDR was considered if the patients had one or both of the following: neovascularization or vitreous/preretinal hemorrhage. Patients with PDR were classified as "active" if they were still receiving treatment and "stable" if they had completed their treatment. Macular edema was detected by OCT images which were acquired simultaneously with the photographic fundus images. Image quality was assessed by retina specialists; if images were unfocused or unclear due to media opacity, which affects the visualization of fine retinal de-

tails and pathology such as microaneurysms, pupil dilation was carried out in an attempt to improve the image quality. If the image was still unclear despite pupil dilation, the patient was referred to the ophthalmology clinic for a detailed dilated funduscopic examination by a retina specialist.

All patients were classified according to their clinical condition into six groups. The first group included patients with no DR, while the second group were patients with NPDR. The third group consisted of patients who had NPDR with macular edema. The fourth group represented patients with PDR, and the fifth group included patients suffering from both PDR and macular edema. The last group consisted of patients with macular edema alone.

The study was conducted in compliance with the Declaration of Helsinki and approved by the Institutional Review Board of the College of Medicine, King Saud University. Patients did not provide informed consent since the study did not compromise anonymity, confidentiality, or breach of the local data protection laws. Additionally, all the collected data were part of routine full assessment investigations for patients who attended the center, and patient consent was not required for these investigations.

Data were analyzed using IBM SPSS version 21 (IBM Corporation, Armonk, NY). The t test was used for differences between independent variables, and the chi-square test was used to assess differences between categorical variables. Values were expressed as means and standard deviations.

RESULTS

Of 2650 patients screened, 1434 patients were excluded. Of the remaining 1216 randomly sampled patients, 207 were excluded; 183 patients were <18 years of age, 19 were suffering from other diabetes types, and five were pregnant females. A total of 1009 patients were eligible for the current study. After excluding 31 patients due to incomplete data, a total of 978 Saudi patients with diabetes were finally recruited for this study (**Figure 1**). The sample included 258 (26.4%) patients with type 1 and 720 (73.6%) patients with type 2 diabetes (**Table 1**) . The mean age for the total sample was 50.5 (16.8) years. Type 1 patients were significantly younger than type 2 patients (P<.001). The mean body mass index was 29.8 (6.0) kg/m^2 for the whole cohort, which was significantly higher than that of the type 2 patients (P<.001). The male-to-female ratio was about 1:1, but more females had type 1 diabetes. The mean duration of diabetes for the total sample was 15.2 (8) years, almost identical for both types. The mean glycated hemoglobin (HbA1c) level was significantly higher among type 1 patients than among type 2 patients (P<.008). Hypertension was significantly more common among type 2 patients than among those with type 1 diabetes (P<.001). Among type 2 patients, only 5.2% were using insulin alone, while 54.4% were using hypoglycemic agents alone.

Slightly less than half (45.4%, n=426) of the screened patients had DR, and 1.9% had macular edema. The majority of patients with DR had NPDR, while PDR contributed to only 12.4% of the total DR patients (**Table 2**). Only 8.5% of NPDR patients had the severe form of the disease, while the remainder had mild or moderate forms. For PDR patients, 52.7% had stable treated PDR, while 30.9% had active PDR warranting either laser treatment or other therapeutic options. Among PDR cases, 16.4% were newly diagnosed as active PDR cases. Among the 426 patients with DR, 154 patients (36.2%) had hypertension. In contrast, 9 patients with macular edema (45.7%) had hypertension.

Of all screened patients who were referred for clinical screening, 10.5% had unclear images. Patients with PDR were significantly older than those with NPDR or normal subjects (mean age [SD]: 47.1 [16.8] years for NPDR, 58.0 [12.2] years, 58.8 [16.1] years for ME), ANOVA F=7.06, P<.001 across all six groups). There were more females among macular edema subjects, severe NPDR subjects, and newly discovered PDR
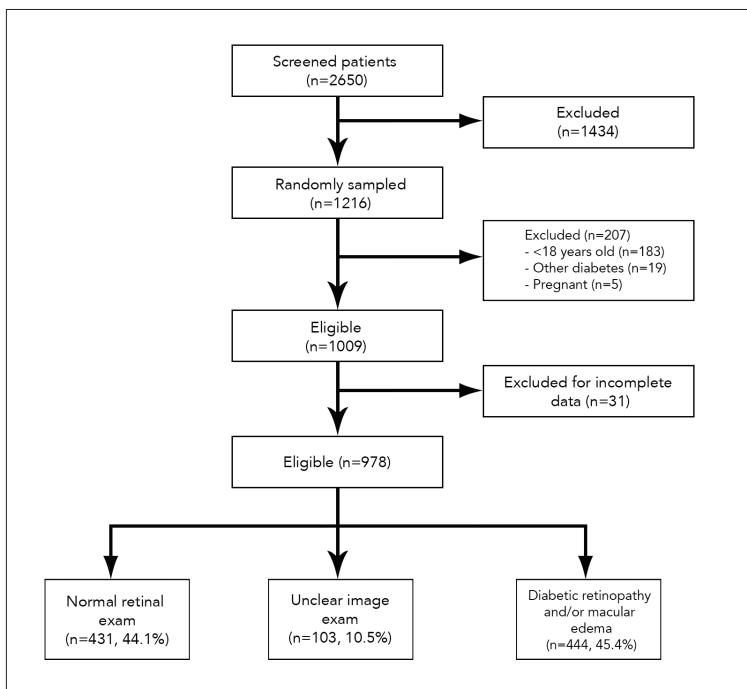
Figure 1. Study flowchart.

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cases. In general, the presence of DR was more prevalent among type 1 patients (55.4%). However, the presence of NPDR was more prevalent in type 2 patients regardless of retinal disease severity. Patients with type 2 diabetes had a higher prevalence of PDR (14.7% versus 7.2%), including stable treated PDR cases as well as new active cases. Moreover, there was a clear preponderance of macular edema among type 2 patients (85.7%).

The duration of diabetes was longer among patients with NPDR and PDR compared with those without DR. The mean HbA1C level was higher in patients with DR and even higher among PDR patients when compared to patients with NPDR. Furthermore, patients with macular edema also had a higher mean HbA1c level than patients without DR. Severe NPDR was more frequent among patients who were using insulin with or without oral agents when compared with those on oral agents alone (3%). In contrast, PDR was more prevalent among patients who used both insulin and oral agents when compared with those who were using insulin alone.

HbA1c and diabetes duration seemed to correlate in their relationship with disease severity. Patients without DR had the lowest HbA1c while those with PDR with macular edema had the highest levels of HbA1c (**Figure 2 bottom**). The mean HbA1c level increased from levels in patients with NoDR and NPDR compared to patients with NPDR with macular edema or PDR, reaching a maximum for patients with macular edema and PDR (ANOVA, F=10.0, P<.001). All differences P<.001 or ≤.05 with post-hoc comparisons vs no DR; other comparisons not statistically significant except for NPDR vs PDR.ME, P=.019). Dilating the pupil improved the quality and area of retinal images. Graphically, the trend in HbA1c seemed to be reflected in the differences in diabetes duration with disease severity, although DR was more common after 15 years of diabetes (**Figure 2 top**).

DISCUSSION

With the retinal screening system used in this study, 45.4% of patients had diabetic retinopathy. This system captured more than 10% of patients who were experiencing a threat to their vision in the form of either macular edema or PDR, which is consistent with the results of similar Brazilian and Scottish studies.[10,11] In Italy, using telemedicine screening programs for retinal disease, DR prevalence was found to be 27.6%,[12] which is similar to a large, 17-year-old community-based DR screening program reported by Misra et al in the UK.[14] In the UK community-based DR screening program, 0.9% of participants had PDR, while 5.7% had macular edema.

Table 1. Demographic and clinical data of the cohort (n=978).

	Total	Type 1 diabetes (n=258, 26.4%)	Type 2 diabetes (n=720, 73.6%)
Age (years)	50.5 (16.8)	28.9 (8.8)	58.3 (11.3)
Age category (years)			
<25	98 (10)	93 (36.1)	5 (0.7)
25-45	227 (23.2)	151 (58.5)	76 (10.5)
46-65	484 (49.5)	14 (5.4)	470 (65.3)
>65	169 (17.3)	0 (0)	169 (23.5)
Height (cm)	161.7 (9.3)	162.5 (9)	161.5 (9.5)
Weight (kg)	77.8 (16.2)	70.6 (15.8)	80.3 (15.5)
Body mass index (kg/m²)	29.8 (6)	26.7 (5.4)	30.9 (5.9)
Body mass index group			
<25	202 (20.7)	103 (39.9)	99 (13.7)
25-30	360 (36.8)	98 (38)	262 (36.4)
>30	416 (42.5)	57 (22.1)	359 (49.9)
Sex			
Men	478 (48.9)	116 (45)	362 (50.3)
Women	500 (51.1)	142 (55)	358 (49.7)
Diabetes duration (years)	15.2 (8)	14.3 (6.8)	15.6 (8.4)
Diabetes duration group			
1-5 years	112 (11.5)	24 (9.3)	88 (12.2)
5-10 years	198 (20.2)	58 (22.5)	140 (19.5)
>10 years	668 (68.3)	176 (68.2)	492 (68.3)
Glycated hemoglobin (%)	8.7 (1.7)	8.9 (1.8)	8.6 (1.7)
Glycated hemoglobin (%) group			
<7	157 (16.1)	28 (10.9)	129 (17.9)
7-8.9	450 (46)	125 (48.4)	325 (45.2)
9-10	183 (18.7)	46 (17.8)	137 (19)
>10	188 (19.2)	59 (22.9)	129 (17.9)
History of hypertension	367 (37.5)	17 (6.6)	350 (48.6)
Management			
Oral hypoglycemic agents	392 (40.1)	0 (0)	392 (54.4)
Insulin	242 (24.7)	205 (79.5)	37 (5.2)
Both	344 (35.2)	53 (20.5)	291 (40.4)

Data are mean (standard deviation) or number (percentage).

Table 2. Ophthalmic screening findings.

	Normal (n=431, 44.1%)	Total	Diabetic retinopathy 426 (43.5%)								Unclear image (n=103, 10.5%)
			NPDR (n=370, 87.1%)				All PDR (n=56)	PDR (n=55, 12.9%)		PDR (n=10)	
			All NPDR	Mild (n=168)	Moderate (n=166)	Severe (n=36)		Stable (n=29)	Active (n=17)		
Age (years)	49.2 (16.1)	48.6 (16.9)	47 (17)	45.5 (17.3)	48.7 (16.2)	46.3 (18.4)	55.8 (13.3)	56.4 (12.3)	60.6 (11.2)	44.7 (13.6)	36.9 (13.1)
Age group (years)											
<25	43 (10)	54 (12.1)	52 (96.3)	28 (53.8)	17 (32.7)	7 (13.5)	1 (1.9)	0 (0)	0 (0)	1 (100)	1 (1)
25–45	108 (25)	114 (25.6)	103 (90.4)	46 (44.7)	46 (44.7)	11 (10.6)	9 (7.9)	6 (6.7)	1 (11.1)	2 (22.2)	5 (4.8)
46–65	225 (52.2)	214 (48.1)	171 (79.9)	76 (44.4)	81 (47.4)	14 (8.2)	33 (15.4)	17 (51.5)	10 (30.3)	6 (18.2)	46 (44.7)
>65	55 (12.8)	63 (14.2)	44 (69.8)	16 (36.4)	23 (52.3)	5 (11.3)	12 (21.8)	6 (50)	6 (50)	0 (0)	51 (49.5)
Sex											
Male	209 (48.5)	227 (51)	190 (83.7)	84 (44.2)	90 (47.4)	16 (8.4)	29 (12.8)	14 (48.3)	11 (37.9)	4 (13.8)	42 (40.8)
Female	222 (51.5)	218 (49)	180 (82.6)	82 (45.5)	77 (42.8)	21 (11.7)	26 (11.9)	15 (57.7)	6 (23.1)	5 (19.2)	61 (59.2)
Body mass index (kg/m^2)	29.5 (5.8)	29.8 (5.9)	29.8 (5.9)	29.4 (5.5)	30.1 (5.9)	30.2 (8)	29.7 (5.4)	30.4 (4.9)	28.8 (5.9)	22.9 (6.2)	30.4 (7)
Body mass index group											
<25	89 (20.6)	92 (20.7)	77 (83.7)	35 (45.5)	32 (41.5)	10 (13)	13 (14.1)	6 (46.2)	5 (38.4)	2 (15.4)	21 (20.4)
25-30	168 (39)	156 (35)	129 (82.7)	66 (51.1)	53 (41.1)	10 (7.8)	17 (10.1)	10 (58.8)	6 (35.3)	1 (5.9)	37 (35.9)
>30	174 (40.4)	197 (44.3)	164 (83.2)	65 (39.6)	82 (50)	17 (10.4)	25 (12.7)	13 (52)	6 (24)	6 (24)	45 (43.7)
Diabetes type											
Type 1	112 (44.6)	139 (55.4)	126 (90.6)	61 (48.4)	51 (40.5)	14 (11.1)	10 (7.2)	6 (60)	1 (10)	3 (30)	7 (6.8)
Type 2	319 (51)	306 (49)	244 (79.7)	105 (43)	116 (47.6)	23 (9.4)	45 (14.7)	23 (51.1)	16 (35.6)	6 (13.3)	96 (93.2)
Diabetes duration (years)	12 (7.1)	17 (7.4)	16.4 (6.9)	15 (7.5)	17.6 (6.3)	18 (6)	23.1 (6.9)	24.1 (6)	25.2 (6.9)	16.2 (5.3)	19.5 (0)

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Table 2 (cont.). Ophthalmic screening findings.

| | Normal (n=431, 44.1%) | Total | Diabetic retinopathy 426 (43.5%) | | | | | | | | Unclear image (n=103, 10.5%) |
| | | | NPDR (n=370, 87.1%) | | | | PDR (n=55, 12.9%) / All PDR (n=56) | | | | |
			All NPDR	Mild (n=168)	Moderate (n=166)	Severe (n=36)	All PDR (n=56)	Stable (n=29)	Active (n=17)	PDR (n=10)	
Diabetes duration group											
1-5 years	89 (20.7)	19 (4.2)	18 (94.7)	12 (66.7)	6 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (3.9)
5-10 years	119 (27.6)	67 (15.1)	61 (91)	43 (70.5)	14 (23)	4 (6.5)	2 (3)	0 (0)	0 (0)	2 (100)	12 (11.6)
>10 years	223 (51.7)	359 (80.7)	291 (81.1)	111 (38.2)	147 (50.5)	33 (11.3)	53 (14.8)	29 (54.7)	17 (32.1)	7 (13.2)	87 (84.5)
Glycated hemoglobin (%)	8.3 (1.6)	9 (1.8)	8.9 (1.7)	8.7 (1.7)	9.1 (1.7)	9.5 (1.8)	9.2 (2)	9.2 (2.1)	8.7 (1.8)	10.4 (2.1)	8.7 (1.6)
Glycated hemoglobin (%) group											
<7%	97 (22.5)	47 (10.6)	41 (87.2)	22 (53.7)	17 (41.4)	2 (4.9)	5 (10.6)	2 (40)	3 (60)	0 (0)	13 (12.6)
7-8.9%	202 (46.9)	198 (44.5)	165 (83.3)	84 (50.9)	66 (40)	15 (9.1)	24 (12.1)	13 (54.2)	9 (37.5)	2 (8.3)	50 (48.6)
9-10%	83 (19.2)	84 (18.9)	73 (86.9)	29 (39.7)	39 (53.5)	5 (6.8)	7 (8.3)	5 (71.4)	1 (14.3)	1 (14.3)	16 (15.5)
>10%	49 (11.4)	116 (26)	91 (78.4)	31 (34.1)	45 (49.4)	15 (16.5)	19 (16.4)	9 (47.4)	4 (21)	6 (31.6)	24 (23.3)
Presence of hypertension	139 (32.3)	164 (36.9)	129 (78.7)	50 (38.8)	63 (48.8)	16 (12.4)	26 (15.9)	12 (46.2)	12 (46.2)	2 (7.6)	64 (62.1)
Treatment OHA	234 (66.9)	116 (33.1)	99 (85.3)	60 (60.6)	36 (36.4)	3 (3)	10 (8.6)	7 (70)	3 (30)	0 (0)	43 (41.7)
Insulin	102 (44.3)	128 (55.7)	119 (92.9)	54 (45.4)	51 (42.8)	14 (11.8)	8 (6.3)	3 (37.5)	2 (25)	3 (37.5)	12 (11.7)
Both	95 (32.1)	201 (67.9)	152 (75.62)	52 (34.2)	80 (52.6)	20 (13.2)	37 (18.4)	19 (51.4)	12 (32.4)	6 (16.2)	48 (46.6)

Data are mean (standard deviation) or number (percentage). NPDR: non-proliferative DR, PDR: proliferative DR.
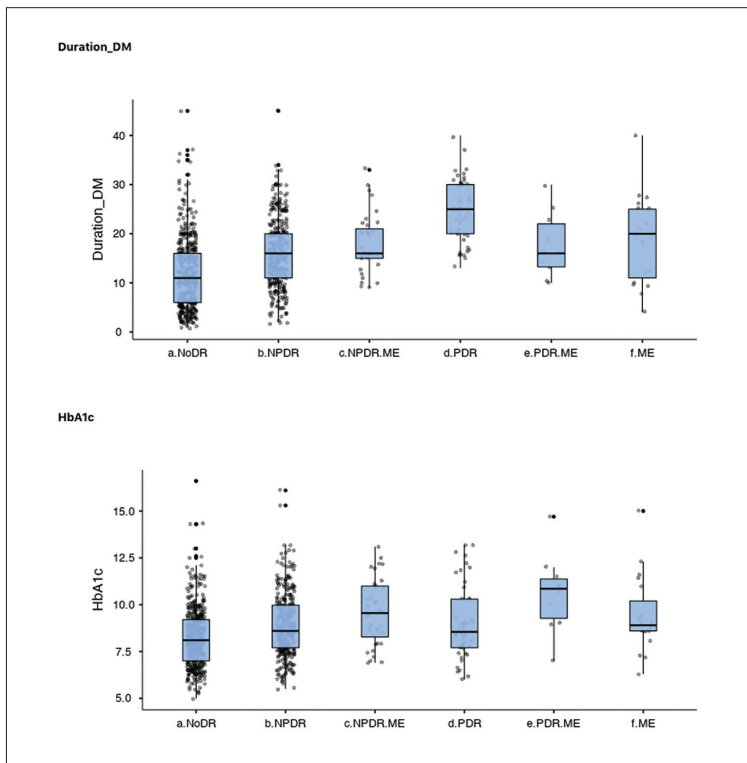
Figure 2. Duration of diabetes (years) and HbA1c levels (%) by diagnosis (No DR: no diabetic retinopathy, NPDR: non-progressive DR, NPDR.ME: non-progressive DR with macular edema, PDR: progressive DR, PDR.ME: progressive DR with macular edema, ME: macular edema alone) (median and interquartile range with outlying data points).

This is lower than the rates observed in our screening program where 12.9% of screened patients had PDR and 1.9% had macular edema. This discrepancy could be explained by the fact that our cohort was selected from a tertiary diabetes center where more complicated cases are expected and because our cohort had a longer diabetes duration and therefore these results are not reflective of the general population.

The screening program in our study was proven to be useful as it detected 30% of cases with active disease that warranted urgent referral for either laser or other therapeutic options. We also monitored more than 50% of patients with stable PDR. These same results were observed in a large longitudinal British study involving more than 20 000 patients, which concluded that screening intervals of up to 24 months would reduce the risk of visual impairment among patients with diabetes.[13] Although Khan et al proved that such a screening program is cost-effective, around 10% of patients would need direct examination by an ophthalmologist as a result of unclear images.[14]

Significant risk factors for DR in our cohort includ-ed old age, especially among patients with PDR. This was also true for macular edema, which could indicate that more frequent screening is needed for older patients. More frequent screening was recommended by the WHO report on the prevention of blindness from diabetes mellitus in 2005.[15] Another significant risk factor in our cohort was gender. Females were found to have more macular edema and newly discovered PDR than males. This is not consistent with observations in the Caucasian population where females had a lower prevalence than males.[16] However, our observation is similar to that reported by a clinic-based retrospective study among the Japanese population, where female gender was an independent risk factor for the development of DR.[17] This could be explained by the effect of pregnancy, which increases the incidence of both DR and macular edema, especially in a cohort with females of childbearing age.[18] Additionally, this could be related to the higher prevalence of type 1 diabetes among female patients in our cohort; type 1 patients are known to have a higher prevalence of DR and ME than patients with type 2 diabetes, especially with increased rates of insulin use.[19]

Among this cohort, patients with type 2 diabetes had a higher PDR prevalence, including stable and active disease, in addition to newly discovered cases. Since type 2 patients contribute to more than 80% of the diabetes population, such data highlight the importance of retinal screening programs.

Patients with DR had higher HbA1c levels, consistent with almost all studies across different ethnicities. The highest HbA1c level was observed among patients with PDR, which holds true for studies of other ethnicities,[20-22] and clearly demonstrates the effect of glycemic control in reducing the incidence of DR among patients with either type 1 or type 2 diabetes. A higher proportion of patients with severe NPDR were found in the insulin-user group with or without oral hypoglycemic agents since this condition usually precedes the development of PDR; therefore, more frequent screening is warranted for patients who are using insulin with or without oral agents than for those who are using oral agents alone.

We found that the most important risk factors for different stages of DR were longer diabetes duration and poor glycemic control reflected by high HbA1c levels. **Figure 2** shows the relationship of these factors with different stages of DR arranged by increasing disease severity. We are unaware of any study that has investigated these two risk factors in relation to DR severity in the Saudi population. Our observation is in line with most studies of different ethnicities that examined these two

risk factors in different DR stages.[23] It is clear that when HbA1c is less than 8.5% and the duration of diabetes is less than 15 years, these risk factors had minimal impact on the presence of DR. The risk for DR and increased severity is clearly increased with longer diabetes duration or higher HbA1c, especially when exceeding 9.5% and 20 years, respectively. This relationship is reported in many epidemiological studies conducted in patients with either type 1 or type 2 diabetes.[24]

When looking at macular edema alone, the risk was still high among patients with higher HbA1c levels and longer diabetes duration. However, HbA1c was lower in this group than in patients with both macular edema and proliferative retinopathy. Our screening program is more likely to detect new cases of DR when HbA1c is higher than 9% and diabetes duration is longer than 15 years. In this study, the value of non-mydriatic funduscopic examination was proven for identifying different stages of DR. Moreover, this screening program allows for early medical or surgical intervention that could save patients' vision and likely reduce the morbidity and costs that may result from vitreous hemorrhage or retinal detachment. Furthermore, in this era of advanced imaging, the use of a user friendly non-mydriatic fundus camera, which acquires a macular OCT image at the same time as the fundus image acquisition, has the advantage of detecting macular edema more accurately when compared to fundus images alone. Our study group believes that the use of OCT should be implemented in screening programs.

A possible limitation is that the study cohort was selected from a tertiary medical center. Moreover, it could also be diagnostically limited by the two fields used in this study, which may have underestimated the number of DR cases since subjects were not exposed to a full mydriatic direct fundus examination by a retinal expert. However, a strength is that our study was an assessment of a practical screening system with the involvement of retinal specialists in reading the fundus photographs and highly trained nurses in screening. Despite the fact that the fundus cameras used were non-mydriatic, dilating the pupil improved the quality and area of retinal images. Although the study was conducted among Saudi patients, the practicality and effectiveness of non-mydriatic funduscopic screening photography for the detection of DR could probably be generalized to patients of other ethnicities with type 1 and type 2 diabetes.

In conclusion, retinal screening programs at the clinical level were found to be useful and practical and could lower healthcare costs by reducing the need for regular ophthalmology clinic visits, especially when large numbers of patients are followed at a hospital-based level. Older patients and insulin users require more frequent screening since they have a higher prevalence of retinopathy, while longer diabetes duration (more than 15 years) and higher HbA1c levels (more than 9%) were confirmed as the most important risk factors for DR and disease severity. A prospective longitudinal study is recommended to disclose the real value of these screening programs to reduce morbidity from chronic diabetes complications such as DR.

REFERENCES

1. Klein BEK. Overview of epidemiologic studies of diabetic retinopathy. Ophthalmic Epidemiol. 2007;14(4):179–83.

2. Yau JWY, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care. 2012;35(3):556–64.

3. Stefánsson E, Bek T, Porta M, Larsen N, Kristinsson JK, Agardh E. Screening and prevention of diabetic blindness. Acta Ophthalmol Scand. 2000;78(4):374–85.

4. Squirrell DM, Talbot JF. Screening for diabetic retinopathy. J R Soc Med. 2003;96(6):273–6.

5. Bourne RRA, Flaxman SR, Braithwaite T, Cicinelli MV, Das A, Jonas JB, et al. Magnitude, temporal trends, and projections of the global prevalence of blindness and distance and near vision impairment: a systematic review and meta-analysis. Lancet Glob Health. 2017;5(9):e888–97.

6. Siu SC, Ko TC, Wong KW, Chan WN. Effectiveness of non-mydriatic retinal photography and direct ophthalmoscopy in detecting diabetic retinopathy. Hong Kong Med J Xianggang Yi Xue Za Zhi. 1998;4(4):367–70.

7. Rohan TE, Frost CD, Wald NJ. Prevention of blindness by screening for diabetic retinopathy: a quantitative assessment. BMJ. 1989;299(6709):1198–201.

8. American Diabetes Association. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018;41(Suppl 1):S13–27.

9. Wilkinson CP, Ferris FL, Klein RE, Lee PP, Agardh CD, Davis M, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology. 2003;110(9):1677–82.

10. Vujosevic S, Pucci P, Casciano M, Daniele A, Bini S, Berton M, et al. A decade-long telemedicine screening program for diabetic retinopathy in the north-east of Italy. J Diabetes Complications. 2017;31(8):1348–53.

11. Cunha LP, Figueiredo EA, Araújo HP, Costa-Cunha LVF, Costa CF, Neto J de MC, et al. Non-Mydriatic Fundus Retinography in Screening for Diabetic Retinopathy: Agreement Between Family Physicians, General Ophthalmologists, and a Retinal Specialist. Front Endocrinol. 2018;9:251.

12. Scottish Diabetic Retinopathy Screening (DRS) Collaborative. Scottish Diabetic Retinopathy Grading Scheme 2007 [Internet]. Scottish Diabetic Retinopathy Screening (DRS) Collaborative. [cited 2019 Feb 28]. Available from: http://www.ndrs-wp.scot.nhs.uk/

13. Misra A, Bachmann MO, Greenwood RH, Jenkins C, Shaw A, Barakat O, et al. Trends in yield and effects of screening intervals during 17 years of a large UK community-based diabetic retinopathy screening programme. Diabet Med J Br Diabet Assoc. 2009;26(10):1040–7.

14. Khan T, Bertram MY, Jina R, Mash B, Levitt N, Hofman K. Preventing diabetes blindness: cost effectiveness of a screening programme using digital non-mydriatic fundus photography for diabetic retinopathy in a primary health care setting in South Africa. Diabetes Res Clin Pract. 2013;101(2):170–6.

15. World Health Organization. Prevention of blindness from diabetes mellitus: report of a WHO consultation in Geneva, Switzerland, 9-11 November 2005 [Internet]. Geneva: Geneva?: World Health Organization; 2006 [cited 2018 Sep 4]. Available from: http://apps.who.int/iris/handle/10665/43576

16. Vujosevic S, Midena E. Diabetic Retinopathy in Italy: Epidemiology Data and Telemedicine Screening Programs. J Diabetes Res. 2016;2016:3627465.

17. Kajiwara A, Miyagawa H, Saruwatari J, Kita A, Sakata M, Kawata Y, et al. Gender differences in the incidence and progression of diabetic retinopathy among Japanese patients with type 2 diabetes mellitus: a clinic-based retrospective longitudinal study. Diabetes Res Clin Pract. 2014;103(3):e7-10.

18. Egan AM, McVicker L, Heerey A, Carmody L, Harney F, Dunne FP. Diabetic retinopathy in pregnancy: a population-based study of women with pregestational diabetes. J Diabetes Res. 2015;2015:310239.

19. Al-Rubeaan K, Abu El-Asrar AM, Youssef AM, Subhani SN, Ahmad NA, Al-Sharqawi AH, et al. Diabetic retinopathy and its risk factors in a society with a type 2 diabetes epidemic: a Saudi National Diabetes Registry-based study. Acta Ophthalmol (Copenh). 2015;93(2):e140-147.

20. Liu Y, Yang J, Tao L, Lv H, Jiang X, Zhang M, et al. Risk factors of diabetic retinopathy and sight-threatening diabetic retinopathy: a cross-sectional study of 13 473 patients with type 2 diabetes mellitus in mainland China. BMJ Open [Internet]. 2017;7(9). Available from: http://bmjopen.bmj.com/content/7/9/e016280.abstract

21. Hermann JM, Hammes H-P, Rami-Merhar B, Rosenbauer J, Schütt M, Siegel E, et al. HbA1c variability as an independent risk factor for diabetic retinopathy in type 1 diabetes: a German/Austrian multicenter analysis on 35,891 patients. PloS One. 2014;9(3):e91137.

22. Long M, Wang C, Liu D. Glycated hemoglobin A1C and vitamin D and their association with diabetic retinopathy severity. Nutr Diabetes. 2017;7(6):e281.

23. Ting DSW, Cheung GCM, Wong TY. Diabetic retinopathy: global prevalence, major risk factors, screening practices and public health challenges: a review. Clin Experiment Ophthalmol. 2016;44(4):260–77.

24. Fong DS, Aiello L, Gardner TW, King GL, Blankenship G, Cavallerano JD, et al. Retinopathy in diabetes. Diabetes Care. 2004;27 Suppl 1:S84-87.