

Delay in seeking medical care after the onset of symptoms in patients with sight-threatening diabetic retinopathy

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Abstract

Background

Diabetic retinopathy (DR) is a common diabetes-associated complication and a primary cause of blindness. One of the critical factors affecting timely and effectual therapy for DR is the delay in treatment after the onset of symptoms. The present study aimed to investigate the reasons for the delay in the treatment of the condition and the risk factors associated with the delay.

Methods

We retrospectively reviewed data from 127 patients with sight-threatening diabetic retinopathy (STDR) treated at Qilu Hospital of Shandong University in China. Various forms of STDR were identified including severe non-proliferative DR, clinically significant macular edema (CSME) and proliferative DR(PDR). Information concerning demography, clinical, and socioeconomic status of the patients was gathered. Risk factors associated with the delay was evaluated using logistic regression analysis.

Results

Among 127 patients with STDR, 89.2% sought medical care one month after the onset of symptoms. Patients who sought for treatment 6 months post-symptom onset had significantly lower income and less knowledge about diabetic eye complications than those presenting within 6 months. Multivariate logistic regression analysis showed that never or infrequent routine examination for diabetic complications was associated with a long delay in seeking medical care (odds ratio 3.06, 95% CI 1.05-9.19, $p < 0.05$; odds ratio 2.91, 95% CI 1.04-8.40, $p < 0.05$).

Conclusions

Most STDR patients sought medical care one month after the onset of symptoms. Never or infrequent routine examination for diabetic complications was associated with a long delay. The results of the present study stress the necessity to implement educational programs on diabetic complications to encourage early medical care and prevent disastrous outcomes.

Background

Diabetes mellitus (DM) is a common chronic systemic disorder with a high global prevalence. Current estimations by the International Diabetes Federation projects that there will be 439 million diabetes patients by 2030 and 642 million by 2040 [1]. Diabetic retinopathy (DR) is a microvascular complication associated with diabetes and a primary cause of visual impairment as well as blindness. Almost all type 1 and over 60% of type 2 diabetic patients acquire some level of DR following 20 years of having the condition [2, 3]. Currently, two grading systems are used for diabetic abnormalities classification: The Early Treatment Diabetic Retinopathy Study classification (ETDRS) and the National Screening Committee (NSC) [4, 5]. Nonappearance of DR is classified as 'R0' (NSC) or '10' (ETDRS). Small retinal hemorrhages and aneurysms can advance to mild non-proliferative diabetic retinopathy (NSCR1, ETDRS 20–35), or to moderate to severe non-proliferative diabetic retinopathy (NSC R2, ETDRS 43–53), and finally to proliferative diabetic retinopathy (NSC R3, ETDRS ≥ 61). Approximately one in ten diabetes patients will develop sight-threatening DR(STDR), including severe non-proliferative DR, clinically significant macular edema (CSME), and proliferative DR(PDR), which could cause severe visual impairment or even permanent loss of vision if not treated [4, 5].

Countries with low- and middle-income accounts for approximately 75% of the global diabetes burden. Besides, 45% of the global diabetic patients are found in India, Bangladesh, Indonesia and China alone [6]. A recent epidemiological study among diabetic patients in China put DR prevalence at 27.9%, and STDR prevalence at 12.6% [7]. DR can be prevented by regulating blood glucose [8] as well as blood pressure [9]. Laser treatment is effectual [10]. Also, vascular endothelial growth factor inhibitors can optimize the outcomes of therapy in diabetic maculopathy [11, 12] and proliferative DR [13, 14].

Although there has been a lot of improvements in DR treatment in the recent past, implementing these effective therapies in developing areas of China is still a challenge. One of the main factors affecting timely and efficient treatment is delay by patients in seeking treatment after the onset of DR symptoms. Studies have shown that the delay period between diabetes symptoms onset or appearance of its associated complications and seeking physician intervention significantly raises the risk of diabetic neuropathy, gangrene, foot ulcers, as well as amputations [15, 16]. Therefore, there is a need to explore the factors contributing to this delay, so as to devise new ways of improving the outcomes of diabetic complications. It remains unclear about this association in patients who progress to STDR which could cause permanent loss of vision if not treated timely and properly. The objective of the current study was to determine the time interval between the onset of DR symptoms and seeking medical care in STDR patients and analyze the risk factors that contribute to this delay. These results may help to provide guidance for developing future educational curricula geared towards the prevention of DR and other diabetes-associated complications.

Methods

The present cross-sectional and retrospective study was conducted in Qilu Hospital of Shandong University, one of the biggest medical centers in Shandong Province, between May 2018 and April 2019. Visual acuity examination, fundus photography and optical coherence tomography (OCT) was conducted to determine the grading of DR. Two grading systems were employed for DR classification: The National Screening Committee (NSC) and the Early Treatment Diabetic Retinopathy Study (ETDRS) classifications [4, 5]. The gradings which included severe non-proliferative DR (R2), proliferative DR (PDR, R3) and clinically significant macular edema (CSME, M1) were categorized as sight-threatening diabetic retinopathy (STDR). Exclusion criteria included: (1) patients with communication difficulties (severe hearing loss/cognitive impairment); (2) patients who declined to partake in the investigation. The period between the onset of DR symptoms such as blurred vision, eye floaters, black spots in the area of vision and seeking medical care at their first visit to local clinic or Qilu hospital was recorded. The following delay periods were selected to differentiate between short term and long-term delays after the onset of symptoms: ≤ 1 month, 1–6 months (including 6 months), 6–12 months (including 12 months) and > 12 months.

Data

Self-administered questionnaires were distributed by ophthalmologists to their patients with STDR. We obtained the following data: (1) demographics, e.g. gender, age, education level, per capita monthly income; (2) diabetes information (i.e. the type, duration of sickness from the condition and blood sugar control); (3) information and gradings related to DR; (4) additional diabetic associated complications, e.g. diabetic nephropathy and diabetic neuropathy; (5) other co-morbidities, such as cardiac heart diseases, history of stroke and hypertension; (6) regular examinations of diabetic complications, such as eye and other complications; (7) report and response from family and (8) knowledge about diabetic eye complications.

All patients were made aware of the use of their personal data in this survey and all of them signed informed consent to participate.

Statistics

A descriptive analysis was performed to evaluate the features of the samples. Continuous variables are presented as the mean \pm standard deviation (SD) and the differences were tested with the chi-square test. Kruskal-Wallis H test was applied to analyze the variables that were not normally distributed. Categorical data are presented as numbers and the chi-square/Kruskal-Wallis H tests were employed to analyze the differences in distribution. Ordinal Logistic Regression (OLR) analysis was conducted to determine the characteristics as well as clinical variables that were independently related to the delay between the onset of symptoms and seeking medical care. A univariate analysis was performed firstly to screen the associated variables. Then a multivariate analysis was performed using some possible risk factors in previous literature in addition to the variables acquired from the univariate analysis. All the analyses were completed in R software (version 3.3.2). The “foreign” package was used for constructing the ordinal logistic regression (OLR). All the statistical tests were two-tailed, and $p < 0.05$ was taken as statistical significance.

Results

Characteristics of the study population and the time interval between onset of DR symptoms and seeking treatment

127 questionnaires were collected and considered valid. The mean age of 127 patients is 53.46 years old, 75 (59.1%) were men and eight (6.3%) had Type 1 diabetes. Among these patients, 15 (11.8%) patients sought treatment within a month following DR symptoms onset and 47 (37.0%) patients between 1 to 6 months. However, there were 22 (17.3%) patients seeking medical care between 6 to 12 months and the remaining (33.9%) patients reported a delayed visit of more than 12 months after the symptoms onset (Fig. 1).

Distribution differences between groups classified by the time interval between symptoms onset and seeking medical care

No considerable differences were observed between the four groups concerning gender, age, and education level. Patients who sought treatment > 6 months post symptoms onset had significantly lower income than those who visited within 6 months. The average duration of diabetes of 127 patients with STDR is 10.83 years. Among these patients, 23 (18.1%) patients had severe non-proliferative DR, 92 (72.4%) patients had PDR and 21 (16.5%) patients had CSME. No significant differences were observed in other complications such as diabetic nephropathy, diabetic neuropathy and co-morbidities such as cardiac heart disease, history of stroke and hypertension. Patients who sought treatment > 6 months post symptoms onset had significantly less knowledge about diabetic eye complications than those presenting within 6 months (Table 1).

Table 1

Characteristics of the study population and differences between four groups classified by time interval between symptom onset and seeking medical care

	time interval between symptoms onset and seeking medical care					p
	All(n = 127)	Group 1 (<1 month, n = 15)	Group 2 (1–6 months, n = 47)	Group 3 (6–12 months, n = 22)	Group 4 (> 12 months, n = 43)	
Demographics						
Gender (male/female)	75/52	10/5	30/17	10/12	25/18	
Age (years)	53.46 ± 10.55	51.13 ± 10.62	52.79 ± 11.53	54.50 ± 10.35	54.49 ± 9.65	0.25
Education (primary/high school/college)	46/62/19	3/9/3	16/22/9	10/10/2	17/21/5	0.4276
per capita monthly income (RMB)	2744.09	3093.33	3182.98	2459.09	2288.37	0.0225
Diabetic history						
Type of diabetes (type 1/2)	8/119	1/14	3/44	1/21	3/40	0.98
Duration of diabetes (years)	10.83 ± 6.98	12.1 ± 9.38	10.25 ± 6.98	10.14 ± 5.23	11.06 ± 6.82	0.96
blood sugar control (follow the treatment regimen) (always/regularly/sometimes/never)	34/73/16/4	3/8/4/0	15/30/0/2	7/13/2/0	9/22/10/2	0.06
Diabetic retinopathy information						
Severe non-proliferative diabetic retinopathy	23	4	10	2	7	0.5
Proliferative diabetic retinopathy (PDR)	92	10	31	20	31	0.17
Clinically significant macular edema (CSME)	21	2	6	3	10	0.58
Other complication and co-morbidities						
Diabetic nephropathy (yes/no)	13/114	1/14	4/43	2/20	6/37	0.79
Diabetic neuropathy (yes/no)	4/123	0/15	1/46	1/21	2/41	0.78
Cardiac heart disease (yes/no)	8/119	3/12	4/43	0/22	1/42	0.051
History of stroke (yes/no)	1/126	0/15	1/46	0/22	0/43	0.63
Hypertension (yes/no)	66/61	8/7	24/23	10/11	24/19	0.93
Regular examination for diabetic complication (regularly/occasional/never)	18/71/38	6/7/2	6/25/16	3/11/8	3/28/12	0.031

		time interval between symptoms onset and seeking medical care				p
	All(n = 127)	Group 1 (<1 month, n = 15)	Group 2 (1–6 months, n = 47)	Group 3 (6–12 months, n = 22)	Group 4 (> 12 months, n = 43)	
Response from family						
Report from family (yes/no)	58/69	6/9	24/23	11/11	17/26	0.67
Response (observation/seeking help)	71/56	10/5	27/20	15/7	19/24	0.21
Knowledge about diabetic eye complications (yes/no)	35/92	9/6	19/28	10/11	10/33	0.046

Risk factors associated with the delay between the symptoms onset and seeking medical care

A univariate logistic regression analysis was conducted firstly to screen the related variables and showed that the income level (odds ratio 0.99, 95% CI 0.99–0.99, $p < 0.05$) and never or infrequent examination for diabetic complications (odds ratio 3.22, 95% CI 1.12–9.62, $p < 0.05$; odds ratio 3.60, 95% CI 1.33–10.15, $p < 0.05$) were associated with a long delay period from the onset of symptoms to seeking treatment. Then some other risk factors such as education level, duration of diabetes, response from family and knowledge about diabetic eye complications were incorporated into the regression model in addition to the variables obtained from previous univariate analysis. The multivariate logistic regression analysis showed that never or infrequent examination for diabetic complications (odds ratio 3.06, 95% CI 1.05–9.19, $p < 0.05$; odds ratio 2.91, 95% CI 1.04–8.40, $p < 0.05$) were independently related to a long delay in seeking medical care, indicating that those patients who had regular and timely checking of diabetic eye or other complications would seek timely and immediate treatment after the symptoms onset (Tables 2 and 3).

Table 2

Univariate regression analysis assessing the factors associated with the delay in seeking medical care in patients with STDR

		odds ratio	95% CI of odds ratio	p value
Age		1.02	0.99, 1.05	
Sex		1.42	0.75, 2.71	
Education level	primary school	2.08	0.80, 5.47	
	high school	1.61	0.63, 4.13	
	college	Reference		
Income level		0.99	0.99, 0.99	p < 0.05
Duration of diabetes		0.9989	0.9516, 1.0486	
blood sugar control	never	1.86	0.27, 16.07	
(follow the treatment regimen)	sometimes	2.95	0.90, 10.38	
	regular	1.04	0.50, 2.14	
	always	Reference		
Routine examination of diabetic complications	never	3.22	1.12, 9.62	p < 0.05
	sometimes	3.6	1.33, 10.15	p < 0.05
	always	Reference		
Response from family	no	1.21	0.64, 2.30	
	yes	Reference		
Hypertension	no	0.91	0.48, 1.72	
	yes	Reference		
Knowledge about diabetic eye complications (yes/no)	no	1.59	0.77, 3.28	
	yes	Reference		

Table 3

Multivariate regression analysis assessing the risk factors associated with the delay in seeking medical care in patients with STDR

		odds ratio	95% CI of odds ratio	p value
Education level	primary school	1.23	0.40, 3.77	
	high school	1.15	0.42, 3.15	
	college	Reference		
Income level		0.99	0.99, 1.00	
Duration of diabetes		1.02	0.97, 1.07	
Routine examination of diabetic complications	never	3.06	1.05, 9.19	p < 0.05
	sometimes	2.91	1.04, 8.40	p < 0.05
	always	Reference		
Response from family	no	1.62	0.77, 3.46	
	yes	Reference		
Knowledge about diabetic eye complications(yes/no)	no	0.8	0.28, 2.21	
	yes	Reference		

Discussion

The results of the present analysis showed that most of the patients with STDR sought medical care one month following DR symptoms onset. Only 11.8% chose to go to the hospital within one month. 37% of these patients sought treatment between 1 to 6 months. 17.3% waited for more than 6 months and 33.9% reported a delayed visit after more than 1 year. Delay in visit resulted in a delay in diagnosis and treatment, and subsequent development of potentially preventable complications. Norina A Gavan et al demonstrated that delaying more than one month in seeking physician intervention could result in a terrible outcome with regards to foot complications related to diabetes in Romania [15]. Thus we speculate that delayed visit after symptoms of DR onset might be one of the critical reasons for these patients progressing to STDR, the much more severe grading of DR which may cause permanent loss of vision. In addition to delay in seeking medical care, studies showed that delay in follow-up or review can also lead to permanently reduced vision in patients with several chronic eye conditions including DR, glaucoma, age-related macular degeneration and so on [17]. Education programs are needed to reduce delays in both first and follow-up visits.

The socioeconomic status of patients might be one of the contributors to the delayed visit. The results of the present analysis showed that patients who sought treatment after 6 months had significantly lower income than those who visited within 6 months, similar to Weng's reports that low socioeconomic status was associated with increased morbidity and premature death in diabetic patients [18]. Patients with higher income may have more access for health care resources and be easier to get better medical supports, which make them choose to seek immediate medical care

upon the onset of symptoms. And another reason may be that patients with poor economic status tend to go to primary medical care at their first visits, where the eye examination is quite limited in most areas of China.

The multivariate regression analysis demonstrated that never or infrequent examination for diabetic complications are risk factors associated with a long delay between the DR symptoms onset and seeking medical care. National Institute for Health and Care Excellence (NICE) of the UK recommends that people be immediately referred to a local eye screening service on diagnosis of diabetes. Screening should be repeated at least annually. However, many patients with diabetes do not have regular eye examinations, especially in underdeveloped areas in China. This is related to a lack of knowledge of diabetes and diabetes-related complications in diabetic patients. Lack of vital knowledge about the disease and its consequences leads to a mistaken perception that diabetes is not a serious disease. Thus, patients with diabetes tend to neglect the significance of seeking immediate treatment when symptoms of diabetes or its related complications occur. Another cause for the delayed eye examinations may be the physician's attitude towards the diabetic eye and other complications. A study revealed that foot examination was conducted more often by specialists compared with general practitioners [19]. The study by O'Brien et al have shown that educations for physicians can increase the screening examination for patients with diabetic foot [20]. In China, it has become routine to perform screenings of the eye, foot or other complications for most physicians in tertiary hospitals. However, limited screenings are performed in primary hospitals or community health services. Educational programs targeting not only patients but also physicians are urgently needed to provide knowledge about diabetic eye complications including symptoms, recognition, management and consequences. NICE advises that type 1 diabetic adults should receive a structured education program 6 to 12 months following diagnosis and those with type 2 diabetes are offered a structured education program at diagnosis. Children and young diabetic patients should be offered a continuing program of education from diagnosis. The education and training will ask patients to seek early and prompt medical care after the onset of symptoms, promote screening of diabetic eye and other complications and ultimately reduce the delay time and avoid preventable disastrous outcomes.

Conclusions

In conclusion, we showed that most STDR patients sought medical care one month after the onset of DR symptoms. Patients who sought treatment after more than 6 months had significantly lower income and little knowledge about diabetic eye complications than those presenting within 6 months. Never or infrequent examination for diabetic complications were risk factors associated with a long delay between the symptoms onset and seeking medical care. These findings are disturbing and stress the need to effect educational programs on the diabetic eye and other complications to encourage early medical care and prevent disastrous outcomes.

Abbreviations

CSME: Clinical significant macular edema; DM: Diabetes mellitus; DR: Diabetic retinopathy; ETDRS: Early treatment diabetic retinopathy study classification; NPDR: Nonproliferative diabetic retinopathy; NICE: National Institute for health and care excellence; NSE: National screening committee; OCT: Optical coherence tomography; OLR: Ordinal logistic regression; PDR: Proliferative diabetic retinopathy; SD: Standard deviation; STDR: Sight-threatening diabetic retinopathy

Declarations

Acknowledgement

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Authors' contributions

YW and FM performed data collection, data analysis and contributed equally. YC, YL, and XW performed data analysis and manuscript preparation. HG conceptualized this study and therefore oversaw the design, data acquisition and analysis, manuscript preparation, literature search and editing. The manuscript was read and approved by all the authors before submission.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

All procedures used in studies related to human participants were based on the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Ethics approval was obtained in the written and officially signed paper form by the authorities of the Ethical Committee of Qilu Hospital of Shandong University before commencing data collection from patients in the study. The original document from the archive can be provided by the corresponding author on request. And all patients signed informed consent before they were allowed to participate in the present study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

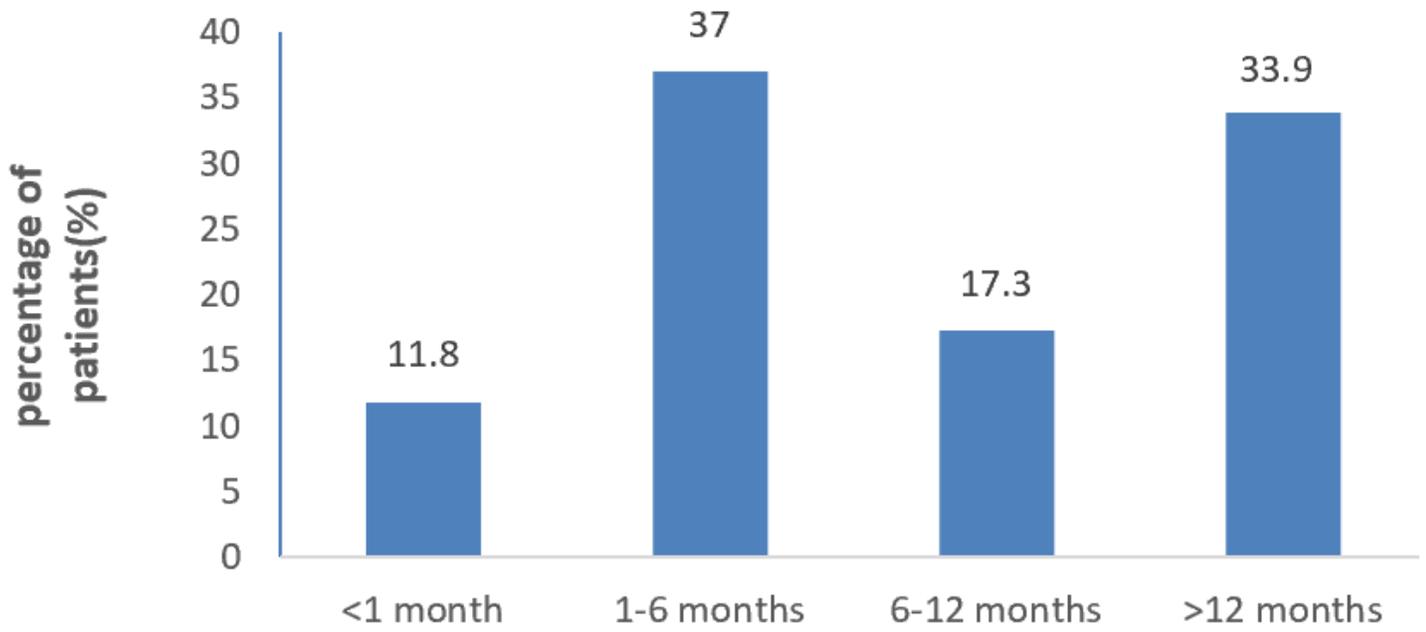


Figure 1

The time interval between onset of symptom of diabetic retinopathy and seeking medical care.