

Prevalence and Associated Factors of Diabetic Retinopathy in People with Type 2 Diabetes Attending Community Based Diabetic Retinopathy Screening in Greater Bandung, Indonesia

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Abstract

Introduction: Determine the prevalence and associated factors of diabetic retinopathy (DR) among people with type 2 diabetes.

Methods: We obtained data of people with type 2 diabetes retrospectively from a community-based DR screening database in Greater Bandung, Indonesia. We encoded the two fields mydriatic 45-degree fundus images to estimate prevalence. The associated factors analysis used multivariate logistic regression.

Result: We screened a total of 4,251 people with type 2 diabetes from January 2016 to December 2019. The overall age-standardised prevalence of any DR was 30.7% (95% CI: 28.7%-32.8%) and vision-threatening DR 7.6% (95% CI: 6.5%-9.0%). The following factors were associated with a higher prevalence of any DR: ages 50+ (OR:1.37; 95% CI:1.05-1.77), duration of diabetes five to ten years (OR:1.38; 95% CI:1.11-1.71) and more than ten years (OR:1.40; 95% CI:1.13-1.73), and postprandial blood glucose 200 mg/dl and higher (OR:1.27; 95% CI:1.03-1.52). The following factors were associated with a higher prevalence of vision-threatening DR: duration of diabetes five to ten years (OR:2.01; 95% CI:1.39-2.91) and more than ten years (OR:1.86; 95% CI:1.28-2.71), postprandial blood glucose 200 mg/dl or higher (OR:1.52; 95% CI:1.05-2.21) and systolic blood pressure 180 mmHg or higher (OR:2.67; 95% CI:1.16-6.17).

Conclusion: Diabetic retinopathy is prevalent among people with type 2 diabetes. People with diabetes should regulate their blood glucose and blood pressure to prevent retinopathy related vision loss.

Keywords: prevalence, diabetic retinopathy, vision-threatening, associated factors, Indonesia

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INTRODUCTION

Diabetes mellitus is a major public health problem, and the number continues to increase.¹⁻³

Globally, the number of people with diabetes was estimated to be 366 million in 2011. That number tends to increase to 578 million by 2030, and 700 million by 2045.^{1,2} Most of the diabetic persons live in low-middle income countries, and they are in productive ages.^{3,4} The growth of diabetic people increases the burden of diabetes-related complications, including Diabetic Retinopathy (DR).⁴

The global prevalence of any DR was 34,6%, and vision-threatening diabetic retinopathy (VTDR) was 10,2%. In number, the burden of DR among people with diabetes is estimated to be 92.6 million, and about 28.4 million of them are threatened to have retinopathy related vision loss.⁴ The number of any DR and VTDR is projected to increase to 191.0 million and 56.3 million, respectively by 2030.⁵ A community-based study in Jogjakarta, Indonesia reported that the prevalence of any DR and VTDR among the population with type 2 diabetes was 43,1% and 26,3% respectively.⁶

DR leads to permanent visual impairment or even blindness if it is left untreated. Development and progression of DR are associated with duration of diabetes, hyperglycemia, and hypertension. Controlling the modifiable associated factors of DR minimise the possible adverse complications.^{7,8}

The Indonesian government has developed a community-Based Chronic Disease Care program, in Bahasa Indonesia "Program Pengelolaan Penyakit Kronis" (Prolanis), to monitor the health status of people with chronic diseases and prevent them from falling to severe complications. The program registers people with hypertension and diabetes in the coverage areas of primary health care services and checks their health parameters regularly.^{9,10}

The Indonesian Eye Center, Cicendo Eye Hospital, Bandung, Indonesia, has been integrating the DR screening program with Prolanis in Greater Bandung, Indonesia, since the year of 2015. Greater Bandung has about 8.5 million population and consists of four districts: Bandung City, Bandung Regency, West

Bandung, and Cimahi. This community-based DR screening is a surveillance approach for the presence of retinopathy among people with diabetes. Our study aims to determine the prevalence and associated factors of DR among people with type 2 diabetes based on the DR screening integrated with Prolanis in Greater Bandung, Indonesia.

METHODS

Ethical considerations

We consulted with The Clinical Research Ethics Committee of The National Eye Center of Indonesia, Cicendo Eye Hospital, Bandung, Indonesia, for ethical aspects of this study. The committee considered that this study evaluated eye care services and analysed the existing data. It, therefore, did not require ethical approval. We informed each patient sufficiently that our study used their data in research anonymously.

Study design and population

Our four years of cross-sectional study obtained data retrospectively from the DR screening database of Prolanis in Greater Bandung, Indonesia. We invited every individual with type 2 diabetes registered in Prolanis for a scheduled DR screening at the Primary Health Services near their areas. The study included all anonymised data of people with diabetes who attended the screening between January 2016 and December 2019. The total participants of 4,251 were included in the study.

Data collections

The study compiled following data: patient's general information (gender and date of birth), diabetes-related health information (duration of diabetes, blood pressure, fasting blood glucose and postprandial blood glucose), and fundus photography details. We input all encoded information in Microsoft Excel sheet for data cleansing. The study recorded only the worst DR status of the participants if they had multiple records.

DR grading and case definition

We used The National Guidelines on Screening for Diabetic Retinopathy in the United Kingdom for DR grading.¹¹ Our study applied the following grading scheme: none (R0), background DR (R1), pre-proliferative DR (R2), proliferative DR (R3), and the presence of maculopathy(M0/M1). We took the worst grade for either eye as the final grading level. The participants who had any stage of DR were defined as an any DR. The patients who suffered from pre-proliferative DR or worse, or Diabetic Macular Edema (DME) at any stage of DR were categorised as a VTDR. The referable cases were patients with VTDR.

The denominator for prevalence estimation was the number of participants with type 2 diabetes in this study.

DR screening procedures

The people with type 2 diabetes who attended the screening were registered. Tropicamide (1%) was applied to each eye. After the pupil was fully dilated, a certified ophthalmic photographer undertook two fields mydriatic 45-degree fundus photography centred on the foveal area and the optic disc using Smartscope Pro portable fundus camera (Optomed, Oulu, Finland). Accredited graders or retina specialists evaluated all retinal images, through a dedicated computer screen, for DR grading and referral decision. We referred the referable cases to the Cicendo Eye Hospital for an adequate treatment.

Statistical analysis

We input All data in STATA 15.1 software (StataCorpLP, College Station, TX) for statistical analysis. We encoded all gradable fundus images for the prevalence of any DR and VTDR estimation. The study presented the prevalence as crude and age-standardised prevalence.

Our study analysed all variables as categorical variables. The following associated factors were the independent variables: age, gender, duration of diabetes, systolic blood pressure, diastolic blood pressure, fasting blood glucose (FBG), and postprandial blood glucose (PPG). The dependent

variables were the presence of any DR and VTDR. The analyses of characteristics of the study population used Pearson Chi-squared, and those with p-values <0.05 indicated statistically significant. The study analysed the association between independent and dependent variables using multivariate logistic regression and presented the results as Odd Ratio (OR) and 95% Confidence Interval (CI). We excluded the participants who had incomplete associated factors data from the multivariate analysis.

RESULTS

From January 2016 to December 2019, a total of 4,251 people with type 2 diabetes, 1,022 (24.0%) males and 3,229 (76.0%) females, were screened by the DR screening team of Cicendo Eye Hospital. Most of the participants were fifty years old and above (n=3,648; 85.8%) and had been suffering from type 2 diabetes for less than five years (n=2,559; 60.2%). (Table 1).

Table 1 Characteristics of study participants

Characteristics	n	%
Gender		
Male	1,022	24.0
Female	3,229	76.0
Ages (years old)		
<50	603	14.2
50+	3,648	85.8
Duration of diabetes (Years)		
<5	2,559	60.2
5 - 10	905	21.3
>10	787	18.5

Prevalence of any DR and VTDR

The overall age-standardised prevalence of any DR within the study population was 30.7% (95% CI: 28.7%-32.8%), VTDR 7.6% (95% CI: 6.5%-9.0%), DME 7.6% (95% CI: 6.4%-8.9%) and PDR 0.5% (95% CI: 0.3%-0.8%). The age-standardised prevalence of any DR in males (32.1%; 95% CI: 27.6%-37.0%) was similar to females (30.3%; 95% CI: 4.69-9.33). The age-standardised prevalence of VTDR in males was 6.6% (95% CI: 4.6%-9.3%), and in females was 8.1% (95% CI 6.7%-9.8%). We present crude and age-standardised prevalence in Table 2.

Table 2 Crude and age-standardised prevalence of diabetic retinopathy in the study population

	Number of Cases	Crude		Age-standardised	
		%	95% CI	%	95% CI
Overall (n=4,251)					
Any DR	1,379	32.4	31.0-33.9	30.7	28.7-32.8
VTDR	361	8.5	7.7-9.4	7.6	6.5-9.0
DME	357	8.4	7.6-9.3	7.6	6.4-8.9
PDR	25	0.6	0.4-0.9	0.5	0.3-0.8
Male (n=1,022)					
Any DR	332	32.5	29.7-35.4	32.1	27.6-37.0
VTDR	72	7.1	5.6-8.8	6.6	4.7-9.3
DME	72	7.1	5.6-8.8	6.6	4.7-9.3
PDR	1	0.1	0.01-0.7	0.1	0.01-0.4
Female (n=3,299)					
Any DR	1,047	32.4	30.8-34.1	30.3	28.0-32.8
VTDR	289	9.0	8.0-10.0	8.1	6.7-9.8
DME	285	8.8	7.9-9.9	8.1	6.6-9.8
PDR	24	0.7	0.5-1.2	0.5	0.3-0.9

DR: Diabetic Retinopathy; VTDR: Vision Threatening Diabetic Retinopathy; DME: Diabetic Macular Edema; PDR: Proliferative Diabetic Retinopathy; CI: Confidence Interval.

Characteristics of the subject with any DR and VTDR

We presented the characteristics of subjects with any DR and VTDR in table 3. Subjects with both any DR and VTDR were more likely to have a longer duration of diabetes and higher PPG. Participants with any DR alone were more likely to be older, while those with VTDR alone were more likely to have higher FBG.

Table 3 Characteristics of the participants with any DR and VTDR

Characteristics	Any DR				p-values	VTDR				p-values
	No		Yes			No		Yes		
	n	%	n	%		n	%	n	%	
Gender										
Male	690	67.5	332	32.5	0.971	950	93.0	72	7.1	0.057
Female	2,182	67.6	1,047	32.4		2,940	91.1	289	9.0	
Ages (years old)										
<50	435	72.16	168	27.9	0.01	548	90.9	55	9.1	0.55
50+	2,437	66.8	1,211	33.2		3,342	91.6	306	8.4	
Duration of diabetes (years)										
<5	1,805	70.5	754	29.5	0.000	2,396	93.6	163	6.4	0.000
5 - 10	613	67.7	292	32.3		813	89.8	92	10.2	
>10	454	57.7	333	42.3		681	86.5	106	13.5	
Blood Sugar (mg/dl)										
FBG										
<120	929	67.7	443	32.3	0.234	1,276	93.0	96	7.0	0.001
120 - <200	1,064	66.1	545	33.9		1,475	91.7	134	8.3	
200+	364	63.75	207	36.3		501	87.7	70	12.3	
PPG										
<200	900	63.2	525	36.8	0.004	1,336	93.8	89	6.3	0.000
200+	544	57.2	407	42.8		851	89.5	100	10.5	
Blood Pressure (mmHg)										
Systolic										
<140	1,789	67.7	853	32.3	0.862	2,427	91.9	215	8.1	0.069
140 - <160	752	66.8	373	33.2		1,023	90.9	102	9.1	
160 - <180	235	67.7	112	32.3		320	92.2	27	7.8	
180+	57	64.0	32	36.0		75	84.3	14	15.73	
Diastolic										
<90	1,979	67.8	939	32.2	0.386	2,671	91.5	247	8.5	0.853
90+	854	66.5	431	33.5		1,174	91.4	111	8.6	

DR: Diabetic Retinopathy; VTDR: Vision Threatening Diabetic Retinopathy; DME: Diabetic Macular Edema; PDR: Proliferative Diabetic Retinopathy; FBG: Fasting Blood Sugar; PPG: Postprandial Blood Sugar

Associated factors analysis

The associated factors analysis of any DR and VTDR was presented in table 4. We included 2365 associated factors data in multivariate logistics

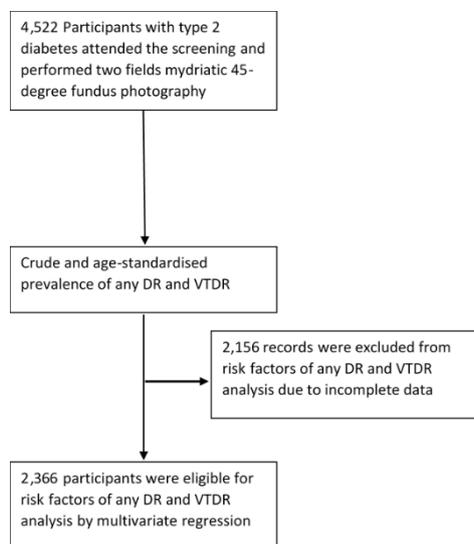


Figure 1 Study Flow Chart

regression. This study excluded 1886 participants who had incomplete associated factors data in the multivariate analysis. (Figure 1)

The following four associated factors were associated with a higher prevalence of any DR: ages 50 years and above (OR:1.37; 95% CI:1.05-1.77), duration of diabetes of 5 to 10 years (OR:1.38; 95% CI:1.11-1.71) and more than ten years (OR:1.40; 95% CI:1.13-1.73), and PPG of 200 mg/dl and higher (OR:1.27; 95% CI:1.03-1.56).

The following four associated factors were associated with a higher prevalence of VTDR: duration of diabetes of 5 to 10 years (OR:2.01; 95% CI:1.39-2.91) and more than ten years (OR:1.86; 95% CI:1.28-2.71), PPG of 200 mg/dl or higher (OR:1.52; 95% CI:1.05-2.21) and systolic blood pressure of 180 mmHg or higher (OR:2.67; 95% CI:1.16-6.17).

Table 4 Associated factors analysis of any DR and VTDR by multivariate logistic regression

Associated factors	Any DR			VTDR		
	OR	p-values	95% CI	OR	p-values	95% CI
Ages (years old)						
<50	1.00		Reference	1.00		Reference
50+	1.37	0.019	1.05 - 1.77	1.02	0.933	0.64 - 1.62
Gender						
Male	1.00		Reference	1.00		Reference
Female	1.06	0.555	0.88 - 1.28	1.3	0.159	0.9 - 1.88
Duration of diabetes (years)						
<5	1.00		Reference	1.00		Reference
5 - 10	1.38	0.004	1.11 - 1.71	2.01	0.000	1.39 - 2.91
>10	1.40	0.002	1.13 - 1.73	1.86	0.001	1.28 - 2.71
FBG (mg/dl)						
<120	1.00		Reference	1.00		Reference
120 - <200	0.98	0.824	0.81 - 1.19	0.94	0.741	0.65 - 1.36
200+	0.94	0.684	0.69 - 1.28	1.25	0.39	0.75 - 2.1
PPG (mg/dl)						
<200	1.00		Reference	1.00		Reference
200+	1.27	0.022	1.03 - 1.56	1.52	0.025	1.05 - 2.21
Systolic blood pressure (mmHg)						
<140	1.00		Reference	1.00		Reference
140 - <160	0.93	0.485	0.75 - 1.15	1.13	0.543	0.77 - 1.66
160 - <180	1.17	0.379	0.83 - 1.64	1.25	0.474	0.68 - 2.29
180+	1.24	0.487	0.68 - 2.28	2.67	0.021	1.16 - 6.17
Diastolic blood pressure (mmHg)						
<90	1.00		Reference	1.00		Reference
90+	1.09	0.388	0.89 - 1.34	0.94	0.736	0.65 - 1.36

DR: Diabetic Retinopathy; VTDR: Vision Threatening Diabetic Retinopathy; DME: Diabetic Macular Edema; PDR: Proliferative Diabetic Retinopathy; FBG: Fasting Blood Sugar; PPG: Postprandial Blood Sugar

DISCUSSION

Community-based DR screening is an effective strategy for finding the cases and facilitating the needed referral.^{12,13} Prolanis is a community-based health program to monitor and manage people with chronic diseases, including diabetes, in the primary level of health care. Prolanis registers the people with diabetic and records their health status regularly.¹⁰ The diabetic registry enables identification of specific population targeted for DR screening. Hence, DR screening integrated with Prolanis ensures diabetic individuals to have regular eye examinations and determine the referable DR.

The Indonesian Eye Centre, Cicendo Eye Hospital, Bandung, Indonesia has a training program for DR graders. The training aims to build the capacities of general ophthalmologists, refractionists and general practitioners to be a qualified DR grader in a community-based screening setting. A successfully trained grader has a good agreement with the retinal specialist for DR grading and referral decisions, so their fundus images interpretation is reliable. In this study, we utilised the certified graders to grade the retinal photography and determine referable cases.

There is a variation of fundus photography application in retinopathy screening. Vujosevic S et al. recommends utilising three fields non-mydratric 45-degree fundus photograph in a screening setting to determine the referable cases. One central non-mydratric 45-degree is used only to verify the presence of DR and DME, and not suitable for DR grading.¹⁴ Piyasena et al. in a systematic review found that both mydratric and non-mydratric retinal photography examinations have an adequate level of sensitivity. Moreover, both one-field and two fields mydratric 45-degree fundus photography are reliable to determine the referable cases.¹⁵ Community-based retinopathy screenings at present commonly utilise one field non-mydratric or two fields mydratric 45-degree fundus photography.¹⁶ In this study, we used two fields mydratric 45-degree focused on the fovea and optic disc as a standard procedure of fundus photography.

The number of people with DR continues to increase in line with the growth of people with diabetes.^{1,17} Among the people with diabetes,

approximately one-third of them suffer from any DR.^{4,18} Even, the studies in Shijiazhuang, China and Jogjakarta, Indonesia found that nearly half of diabetic people had some form of DR.^{6,19} The prevalence of any DR found in this study was 30.74%. This fact represents the magnitude of DR among the diabetic population. The possibility of a permanent vision loss threatens the affected people. It is an urgent need for diabetic individuals to perform eye examination as earliest. Also, the necessity of referring every diabetic person to ophthalmologists ought to be a norm in diabetes care.

The burden of visually impaired people due to DR is increasing, despite the stable prevalence of DR over a decade. This phenomenon is attributed to the growth of population, especially the older people in most countries and the decreasing of the death rate.²⁰ The prevalence of VTDR ranged from around 3% to 11% in some studies.^{4,18,21} In this study, we found 8 out of 100 people with diabetes have a risk progressing to permanent vision loss. Therefore, comprehensive care for DR, including public education, community-based screening and treatment, must be comprehensively integrated with the national health system involving related professional health workforces at all level of the health services.¹²

The duration of diabetes persistently associates with the progression of retinopathy. Some studies, including our study, showed that duration of diabetes more than five years was a strong predictor for the development and progression of retinopathy.^{4,7,19} Therefore, a long-standing diabetic person must be observed very carefully to prevent from retinopathy-related vision loss. Many patients with type 2 diabetes have had years left undiagnosed. The ophthalmologists often discover notable retinopathy at the time of diagnosis. Hence, every adult with diabetes ought to perform comprehensive eye check and dilated pupil examinations regularly.²²⁻²⁴ The American Diabetes Association recommend a comprehensive eye check and initial mydratric retinal examination within five years after the onset of diabetes for adults with type 1 diabetes or at the time of diagnosis for patients with type 2 diabetes.

The mydriatic retinal examination should be repeated every two years if there is no evidence of retinopathy. Patients ought to perform the test annually if an early stage of retinopathy is present. When the retinopathy is worsening or visually threatening, the examinations should be done more often.²⁴

Controlling blood sugar is an essential component in DR management. The association between elevated both FBG and PPG was observed consistently by some studies in China.^{7,19,25} A cohort study in Wales found that the decreased β -cell responsiveness is linked to DR, causing an increase of both FBG and PPG.²⁶ Our study failed to observe an association between the elevation of FBG with both any DR and VTDR. However, we discovered an association between higher PPG with both any DR and VTDR. Similarly, studies in Japan by Shiraiwa T et al. and Takao T et al. found an association between elevated postprandial and progression of DR. The studies suggest that correcting postprandial hyperglycemia is useful for preventing retinopathy, despite a satisfactory level of HbA1c.^{27,28}

Increased blood pressure potentially harms the retinal capillary endothelial cells in the eyes of people with diabetes.²⁹ Some studies showed a consistent association between hypertension and the progression of diabetic retinopathy.^{7,19,21} However, similarly with our findings, countrywide research in the US by Zhang X et al. found that only elevated systolic blood pressure is associated with the presence of DR. The study did not discover any association between the level of diastolic blood pressure and the occurrence of retinopathy.²¹ Ting DSW et al. in a review suggest that every 10 mmHg reduction of systolic blood pressure potentially reduces the risk of retinopathy by 35%, and blindness by 50%.⁵ One of the possible explanations about the role of systolic blood pressure in the advancement of DR is a pulse pressure (the difference between systolic and diastolic blood pressure) alteration.²¹ Some studies found an association between higher pulse pressure with the progress of DR.³⁰⁻³² However, the mechanism of this association is still unclear.³²

We observed some limitation in this study. We only examined the attendees and missed the potential participants who did not come to the screening. Also, in a retrospective data collection, we could not control the data intensely, so some characteristics data were missing. Our study did not evaluate serum HbA1C and lipid profiles because they are not standard tests in Prolanis.

CONCLUSION

The age-standardised prevalence of any DR and VTDR in this study was 30.7% and 7.6% respectively. These findings suggest that DR is prevalent among people with type 2 diabetes. A permanent visual loss threatens people with diabetes if they do not monitor the development and progression of retinopathy. Our study found that duration of diabetes more than five years and PPG more than 200 mg/dl had an association with a higher prevalence of both any DR and VTDR. Age of 50 years and above was associated with development any DR alone, while systolic blood pressure more than 180 mmHg was associated with VTDR alone. Therefore, older people with diabetes should maintain their blood glucose and blood pressure regulated. DR screening integrated with Prolanis is a health system approach that enables people with diabetes to avoid unfavourable events related to the development and progression of DR.

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