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The Accuracy of Detecting Diabetic Retinopathy Using Panoptic Ophthalmoscope by Primary Care Doctors At Klinik Kesihatan Sendayan

***Abstract*—**Diabetic Retinopathy (DR) is a microvascular complications of diabetes that may lead to blindness. The prevalence is increasing which demands early detection to prevent further deterioration of retinopathy However, the gold standard fundus camera is not widely available in primary care. The study assesses the accuracy of PanOptic Opthalmoscope (PO) as a screening tool for DR at primary care level A cross-sectional study on 66 diabetes patients were enrolled via systematic random sampling. The sample size was calculated using PASS software and OpenEpi method. PO and fundus camera were done on the same day with DR screening. PO were done among six primary care doctors. Fundus camera photo was interpreted by the Ophthalmologist as gold standard. Both findings were compared and analysed. PO has low accuracy (53%) in detecting DR.The sensitivity and specificity of DR detection was 10.3 % and 86.5% respectively. The positive predictive value (PPV) was 37.5% and negative predictive value (NPV) was 55.2%. The accuracy of Sight threatening abnormalities (STA) was 75.8%. The sensitivity and specificity of STA were 35.3% and 89.8%, respectively. The PPV was 54.4% and NPV was 80%. The prevalence of newly diagnosed DR was 43.9%, while prevalence of STA was 25.8%. DR is significantly associated with patients living with diabetes for more than 10 years (p = 0.007). The accuracy of PO in DR screening is poor, but it is modestly acceptable for STA detection. However, the sensitivity and PPV is low, making serious retinopathy undetected. The prevalence of DR is higher with increasing duration of diabetes. We recommend the availability of fundus camera in primary care setting.

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1 INTRODUCTION

Diabetic retinopathy (DR) affects 2.6% global blindness in the world[1]. It is also the commonest cause of visual loss in productive age in Malaysia [4,5,7]. It was reported that DR causes 10% of blindness in Malaysia [7]. The prevalence of DR was 11.52% from the National Diabetes Registry (NDR) 2020. Higher prevalence was found from the National Diabetic Eye Registry (NDER) with 36.8%[4,5]. These huge differences could be due to the different settings and methods of screening and detection of DR.

A local study in East Malaysia had found that DR is associated with duration of DM, body mass index (BMI), and visual loss[14]. Furthermore, another local study in Kelantan had found that the significant predictors of proliferative DR were age, duration of DM, nephropathy and peripheral neuropathy[15]. A study from Saudi Arabia had found younger age at onset, longer duration, and insulin use appeared to be the strongest predictors for DR[16]. Another international study had found that diabetic patients after 10 years of disease with poor HbA1c and nephropathy have higher risk of DR in Southern Brazil[17].

Screening for DR was introduced way back since 1997 in primary care setting in Malaysia [27]. The methods used to detect DR had changed from direct ophthalmoscopy to the digital retinal imaging until to the recent evolving teleretinopathy [3-5]. Teleretinopathy combines the medical instrument like non-mydriatic camera for screening with telehealth for patient's consultation that provides convenient and reliable diabetic eye screening [3] . Instruments that are available for DR screening are direct ophthalmoscope, PAN-ophthalmoscope (PO), binocular indirect ophthalmoscope (BIO), slit lamp biomicroscope, mydriatic fundus camera and non-mydriatic fundus camera[4,5]. The United Kingdom (UK) National Institute for Clinical Excellence (NICE) recommends that the screening modalities needs to have a sensitivity

of at least 80% and a specificity of at least 95% with a technical failure less than 5%[18].

A systematic review found ophthalmoscopy used either direct or indirect still has a role in detecting DR, especially in trained clinicians[20]. A local study done in the ophthalmology clinic had found that the sensitivity of PO to detect sight threatening retinopathy was 58.5%, which was lower; as compared to the sensitivity of conventional direct ophthalmoscope (DO) which was 73.2%[22]. However, in this study, the investigator had only 3 months of experience of using PO.

PO was chosen in the study for its promising prospects. It is a handheld direct illumination ophthalmoscope developed by Welch Allyn that provides five time larger fundus view as compared to DO on non-dilated eyes (15).This effect was contributed by better field of vision which allows 26% of better magnification. PO provides 25° field of vision as compared to 5° field of view in DO. It is affordable and costed six times lesser than non-mydriatic fundus camera. It is also a handheld device powered by rechargeable built in lithium battery and allows better distance during examination (15). However, DO is cheaper as compared to PO making DO easily available at primary care as compared to PO. DO was found to have better operability by 1.38 time as compared to PO [22].

Malaysian guideline has recommended that non-mydriatic fundus camera to be used as screening tool for DR whenever possible[4,5]. According to NHMS(2019),68.2% of diabetic patients sought treatment from the Ministry of Health (MOH) health clinics [2]. However, there are only 107 fundus cameras in the whole country to serve 772 health clinics and polyclinics run by medical officers and medical assistants [5,21]. In Negeri Sembilan, there are 11 fundus cameras which were distributed to 11 health clinics out of 45 health clinics[5]. If there is no access to fundus camera, ophthalmoscope is used for DR screening [4,5,21].

1.1 Materials and Methods

This was a cross-sectional observational study conducted at Klinik Kesihatan Sendayan, Negeri Sembilan from June 2020 to September 2020. This study was approved by the Malaysian Medical Research Ethic committee (NMRR-20-78-52490) and Jabatan Kesihatan Negeri, Negeri Sembilan (JKNNS). Informed consents were obtained from participants in compliance with the ethical principles outlined in the Declaration of Helsinki and the Malaysian Good Clinical Practice Guidelines. We had to reduce the duration from six to three months due to COVID-19 pandemic and the study site clinic renovation works.

The sample populations were adult diabetic patients aged more than 18 years old treated in Klinik Kesihatan Sendayan. The inclusions criteria were Malaysian citizens or permanent residents, aged 18 and above whom were established with diagnosis of DM, never been diagnosed with diabetic retinopathy and came with an accompanying person. The exclusion criteria were diabetic patients who had been diagnosed with DR, patients who comes alone, have matured cataract or VA worse than 3/60 or acutely unwell such as having fever or respiratory tract illness or vomiting or had moderate to high COVID-19 risk factors.

The sample size calculated based on Power Analysis and Sample Size (PASS) software based on the desired type 1 error, power and effect size[24]. The minimum calculated sample is 50 and final highest calculated sample size was 82[24-25]. In account of about 10% non-respondent, it yields a sample size of 90 patients. However, due to the occurrence of pandemic Covid-19, we only managed to obtain 66 patients. Systematic random sampling was applied in this study.

Primary care doctors selected were all medical officers excluding investigators on duty in the outpatient department of Klinik Kesihatan Sendayan. They received retraining for PO use by a medical officer with 5 years of experience in using the PO. The fundus interpretation was trained by a medical officer who is a certified grader with credentialing and privileging(C&P) in fundus interpretation. The duration of training and practice was 10 months prior to the research. The fundus camera used in this study was VISUCAM 224 model by Zeiss from Germany. It is a non-mydriatic fundus camera with a 24-migapixel sensor.

Patient who was selected via systemic randomised sampling received informed consent by principal investigator. Then visual acuity was done by medical assistant or staff nurse. Following that, two field non-mydriatic fundus photos was taken for each eye of the participants by a trained paramedic or medical officer and saved in a google drive. The saved fundus photo was reviewed by an ophthalmologist to validate the diagnosis. The fundus photo interpretation by the ophthalmologist is the standard setting in this study. The grading of retinopathy is based on the

International Clinical Diabetic Retinopathy and Diabetic Macula Edema Disease Severity Scale as suggested by MOH DR screening [4]. All fundus photos were interpreted by a single ophthalmologist.

PO examination was done by primary care doctors after eye dilatation with tropicamide 1% solution. Every primary care doctor received cumulatively 13 different patients. The principal investigator randomly picked one doctor's name in a piece of paper to determine equal random selection. Comparison was made between PO examination findings by the primary care doctors with the standard setting. The fundus photos taken were blinded from primary care doctors.

The main purpose of this study was to examine the accuracy of the primary care doctors in screening DR. However occasionally other abnormalities other than DR that require referral to the ophthalmologist could be found during the screening. Therefore, other retinal or media abnormalities as stated above were also included as positive findings labelled "abnormal" that required referral. They were defined as sight threatening abnormalities (STA).

The study procedure had been conducted following COVID-19 standard operating procedure proposed by the MOH [26]. The outcomes were the accuracy, sensitivity and specificity of diabetic retinopathy detection by primary care doctors using PO. Factors that were associated with diabetic retinopathy such as age, duration of DM, HbA1c level and nephropathy were recorded.

1.2 Results

1.21 Characteristic and health profile of the study population

The intended number of patients for screening was 192 patients. During the study period, 139 patients (72.4%) came for eye screening. A total of 66 patients with type 2 diabetes mellitus were enrolled in this study. The response rate was 94.3% as 70 patients were invited to participate. The proportion of newly diagnosed diabetic retinopathy based on the standard setting of using non mydriatic fundus camera interpreted by an ophthalmologist was 29 (43.9%). Mild NPDR was detected in 14 patients (21.2%), followed by 10 patients (15.2%) had NPDR with maculopathy, 3 patients (4.6%) had PDR, 1 patient (1.5%) each for PDR and cataract, bilateral cataract and moderate NPDR. 34 patients (51.5%) were diagnosed as normal while 2 patients (3.0%) had other findings. All of the distribution of the patients' specific diagnosis were summarized in table 2.

The mean age of patients was 54.59±2.87 (ranged from 26 to 80 years). 47(71.2%) patients were aged 50 and above. 22(33.3%) patients were male and 44(66.7%) were female. 45(68.2%) were Malays followed by Indians,14 (21.2%) and Chinese, 7 (10.6%). Majority of the patients were married (n=59,89.4%) and had secondary or tertiary education (n=47,71.2%). More than half were employed (n=37,56.1%) with income less than RM4849 (n=60 ,90.9%). All of the demographic findings were summarized in table 3.

Table 1: Proportion of diabetic retinopathy (n=66)

Diabetic retinopathy	Frequency, n (%)
Yes	29 (43.9)
No	37 (56.1)

Table 2 : The patients' specific diagnosis (n=66)

Specific Diagnosis	Frequency, n (%)
Normal	34 (51.5)
Mild NPDR	14 (21.2)
Moderate NPDR	1 (1.5)
NPDR and Maculopathy	10 (15.2)
PDR	3 (4.6)
PDR and cataract	1 (1.5)
Cataract	1 (1.5)
Others	2 (3.0)

Table 3: The Demographic Profile of the participants (n=66)

Variables	Frequency, n (%)
Gender	
Male	22 (33.3)
Female	44(66.7)
Age	
<50 years old	19(28.8)
≥50 years old	47(71.2)
Ethnicity	
Malay	45(68.2)
Chines	7(10.6)
Indian	14(21.2)
Marital status	
Married	59(89.4)
Divorced/widowed	7(10.6)
Education level	
Up to primary education	19(28.8)
Secondary or Tertiary	47(71.2)
Employment	
Employed	37(56.1)
Unemployed	29(43.9)
Household income	
<RM4849 (B40)	60 (90.9)
RM4850-RM10959 (M40)	5(7.6)
>RM10960 (T20)	1 (1.5)

The duration of known diabetes status ranged from 1 year to 30 years. The median duration of diabetes was 6 years with majority diagnosed with DM more than 10 years (n=47,71.2%). Most patients had hypertension (n=53,80.3%), dyslipidemia(n=54,81.8%), obesity (n=40, 60.6%) and family history of diabetes mellitus (n=51,77.3%). The findings of other associated factors such as nephropathy, neuropathy, ischemic heart disease and history of stroke were summarized in table 4.

Majority patients had suboptimal HbA1c (n =50,75.8%), normal eGFR ≥60 (n= 64,97%) and BMI >27.5 (n=40,60.6%). Almost half of the participants had optimal blood pressure (n=37,56.1%), without albuminuria (n=36,54.5%) and normal eye sight (n=34,51.5%) (Table 4).

Table 4: The Health profile of the participants (n=66)

Variables	Frequency, n (%)
Duration of DM	
<10 years	47(71.2)
≥10 years	19(28.8)
Hypertension	
Yes	53(80.3)
No	13(19.7)
Dyslipidemia	
Yes	54(81.8)
No	12(18.2)
Obesity	
Yes	40(60.6)
No	26(39.9)
Smoking	
Yes	15(22.7)
No	51(77.3)
Known Family History	
Yes	51(77.3)
No	15(22.7)
Nephropathy	
Yes	29(43.9)
No	37(56.1)
Neuropathy	
Yes	7(10.6)
No	59(89.4)
IHD	
Yes	3(4.5)
No	63(95.5)
Stroke	
Yes	3(4.5)
No	63(95.5)
HbA1c	
Optimal (≤7.0mmol/L)	16(24.2)
Suboptimal (>7mmol/L)	50(75.8)
BP	
Optimal (≤135/85)	37(56.1)
Suboptimal (>135/85)	29(43.9)
LDL	
<2.7mmol/L	31(47.0)
≥2.7mmol/L	35(53.0)
eGFR	
≥60	64(97)
<60	2(3.0)
Albuminuria	
Yes	30(45.5)
No	36(54.5)
BMI	
<22.9	5(7.6)
23-27.5	21(31.8)
>27.5	40(60.6)
Visual acuity	
Normal	34(51.5)
Mild (6/12-6/18)	19(28.7)
Moderate (6/18-6/60)	13(19.7)

*Visual acuity classification is based on International classification of Diseases 11(2018) [16]

1.22 Factors associated with diabetic retinopathy

The duration of type 2 diabetes mellitus was significantly associated with the presence of diabetic retinopathy in the univariate analysis (p=0.007). Other factors associated with DR were not significant.

1.23 Accuracy, Specificity and Sensitivity

The accuracy of PO in detecting DR was 53% while the accuracy of PO in detecting abnormality that requires referral was 75.76 %. Therefore, PO is not accurate for DR detection but modestly accurate for sight threatening abnormalities detection and referral. The proportion of newly diagnosed DR was 29 (42.42%). The sensitivity of PO for DR detection was 10.7% and the specificity was 86.8%. The positive predictive value (PPV) and negative predictive value (NPV) was 37.5% and 55.2% respectively. The reference standard used was the non-mydratic fundus photo interpretation by an ophthalmologist. 26 (89.66%) diabetic retinopathy cases were missed. (Refer Table 5).

Table 5: The detection of Diabetic Retinopathy (DR) with PanOptic Opthalmoscope (PO)

		Reference standard		
		DR	No DR	Total
Diagnosis PO	DR	3	5	8
	No DR	26	32	58
Total		29	37	66

A total of 17 patients were indicated for referral to the Ophthalmology clinic. Fourteen (82.35%) referal for sight threatening DR which were NPDR with maculopathy in 10 patients (58.82%) and PDR in 1 patient (5.88%) that had cataract as finding on left eye. One patient had bilateral eye cataract and 2 patients (17.64%) had other findings (ie: Age Related Macular Retinopathy and geographic atrophy respectively).

The sensitivity of panoptic funduscopy for STA that requires referral was 35.3% and the specificity was 89.8%. The PPV and NPV was 54.5% and 80.0% respectively. The result showed 11 (64.7%) patients require referral was missed. (Refer Table 6).

Table 6: The detection of STA with PO that requires referral

		Reference standard		
		Refer	Do not refer	Total
PO findings	Refer	6	5	11
	Do not refer	11	44	55
Total		17	49	66

2 DICUSSION

Diabetic retinopathy (DR) is one of the important complications arising from diabetes mellitus. The high prevalence of 36.8% of DR from the National Diabetic Eye Registry in 2007 showed the high burden of DR[8]. National Diabetic Registry (NDR) which collected data from primary care setting reported 11.52% diabetic patients having DR in 2020. NDR data are from primary care level and did not include patients from the ophthalmology clinic [13]. The usage of screening tool for DR in each primary care setting maybe different from one another in which some clinics might use fundus camera for detection of DR, while other clinics used direct ophthalmoscopy. This explained the possibility of DR being missed in primary care setting.

Our study discovered a high proportion of newly diagnosed DR (n=28,42.4%) which was higher than the prevalence of DR in Malaysia in year 2007 (36.8%). This number of newly diagnosed DR was much higher compared to the proportion of DR in Klinik Kesihatan (KK) Sendayan as reported from NDR 2019 which was 10.42%[23]. Diabetic eye screening at KK Sendayan uses PO which may contributed to a lower DR detection rate. In this study, a diagnosis of DR was made if any eye of the participants had any diabetic retinopathy changes detected by the fundus camera which was interpreted by the ophthalmologist. Due to some limitations, we could not enroll a higher number of participants in this study. Perhaps, a higher number of newly diagnosed DR maybe detected if more samples were included. However, the proportion of newly diagnosed DR of 43.9% in this study was higher than 29.2% from a previous study at Kuala Lumpur [11].

This study showed the usage of PO among medical officers in Klinik Kesihatan Sendayan had low sensitivity with 10.7% but high specificity of 86.8%. The finding in our study was lower than the acceptable value by NICE guideline which is sensitivity of 80% and specificity of at least 95%[18].The accuracy of DR detection using PO in this study was low with 54.56%. The low sensitivity of the study may attributed to lack of experience in handling the PO and the limitation of PO that might miss the periphery view. Patient factor also plays a role as poor cooperation by the patient can attributes to difficulty to perform the PO and interpret the finding. The skill on manoeuvring the PO requires experience in order to perform better.

The sensitivity to detect sight threatening abnormalities (STA) requiring referral was 35.3% while the specificity was 89.8%. The finding was much lower compared to a study done in Sarawak Malaysia that found the sensitivity to detect sight threatening retinopathy with panoptic ophthalmoscope was 53.5%[22]. The study however was conducted by a single investigator who is an ophthalmologist[22]. It is found that the accuracy for detecting sight threatening abnormalities (STA) requiring referral with PO was modestly acceptable with 75.65%. However, the sensitivity is 35.3% in detecting STA which is considered low.

An effective screening tool especially in the community requires high sensitivity rate in order not to miss disease detection. Even though we found a high specificity of in screening DR by the medical officers, the lower sensitivity implied that usage of PO is not reliable as a screening tool in

primary care due to high false negative result. However, as a screening tool for sight threatening abnormalities, PO gives a modest accuracy and specificity. The sensitivity is still lower than the standard suggested by NICE guideline [18].

In this study, duration of more than 10 years of having diabetes was found to be significantly associated with DR (p =0.007). This finding was in accordance with findings of previous local and abroad researches that studied the association of DR with duration of diabetes. A local study in east Malaysia had found that DR was associated with duration of DM, body mass index (BMI), and visual loss[14]. Furthermore, a study in Kelantan had found that the significant predictors of proliferative diabetic retinopathy were age, duration of DM, nephropathy and peripheral neuropathy[15]. A study from Saudi Arabia had found younger age at onset, longer duration, and insulin use appeared as strongest predictors for diabetic retinopathy[16]. Another international study had found that diabetic patients after 10 years of disease with poor HbA1c and nephropathy have higher chance of DR in Southern Brazil[17].

However, this study was unable to find any association of DR with other factors that had been studied, most likely due to small sample size. Perhaps, a different finding maybe obtained with recruitment of larger sample size in this study.

3 LIMITATIONS

The study was conducted during Pandemic COVID-19 and the study site was temporarily closed for internal renovation for almost three months. We were unable to get more participants to reach our sample size target as we need to minimize the medical officers' contact with the participants.

The six medical officers who conducted the procedure has a range of 2 to 5 years of experience with PO. The interrater reliability and intra-observer agreement among the six medical officers who performed the PO was not calculated in view of all medical officers reviewed different patients and the fundus photo interpretation was done by one ophthalmologist. The study was conducted during patient's appointment and not all medical officers involved were present during the procedure.

The participants in the study did not represent our diabetic population as a whole as those with established diabetic retinopathy and frail patients were not included in the study due to the inconvenience in dilating the pupil and the risk of fall. Therefore, the study was less likely to include diabetes patients with multiple comorbidities especially those with renal failure, stroke with hemiparesis or patients with amputations. Patients who had resolved albuminuria after treatment with ACE inhibitor or ARB also improved the proportion of microalbuminuria in the study. Some patients who have multiple comorbidities had better HbA1c in view of successful optimization of diabetes care from patients' awareness and motivation.

4 CONCLUSION

From the study, we conclude that PO is not a good screening tool for primary care doctors and sight threatening retinopathy will be missed. Having DM for more than 10 years is significantly associated with DR development and prioritized for diabetic eye screening. The availability of non-mydriatic fundus camera can help in early detection of diabetic retinopathy. With early treatment and optimization of glycemic control, the incidence of visual impairment and blindness among diabetic patients can be reduce.

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