Original article

Agreement on diabetic retinopathy grading in fundus photographs by allied ophthalmic personnel as compared to ophthalmologist at a community setting in Nepal

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Abstract

Introduction: Diabetic retinopathy (DR) is the emerging cause of blindness in the developing world. Timely detection of DR could save vision from its avoidable blinding condition. **Objective:** To assess the accuracy of DR grading in fundus photographs by the allied ophthalmic personnel (AOP) as compared to ophthalmologist at a community setting in Nepal. **Materials and methods:** Fundus photographs of known diabetes subjects attending for DR screening were graded by two groups of AOP and ophthalmologist. Agreement for DR grading by the AOP versus ophthalmologist was assessed using kappa coefficient (*k*). **Results:** Fundus photographs of 864 eyes of 435 subjects with diabetes were evaluated in the study. The agreement was substantial for detection of normal versus abnormal retina by both the AOP 1 and AOP 2. For normal versus abnormal macula, the agreement was substantial for AOP 1 and moderate for AOP 2. The agreement for grading macular exudates, retinal hemorrhage, venous beading ranged from moderate to substantial for both the AOPs. There was overall substantial agreement for diagnosing cases with or without DR and CSME by both the AOP 1 and AOP 2. The agreement ranged from fair to moderate for diagnosing other stages of NPDR by both the AOPs. **Conclusion:** Allied ophthalmic personnel with training could be a first level DR screener and referral of vision threatening DR. Three out of five diabetics could be managed at community level and thus reduce work load of ophthalmologist. This DR screening modality can be useful in other resource limited countries.

Key words: diabetic retinopathy, diagnostic accuracy, Ophthalmological diagnostic technique grading, allied ophthalmic personnel, Ophthalmologist

Introduction

Diabetes mellitus (DM) is an emerging public health problem in the low and middle income countries (Wild et al, 2004). DM is growing as epidemics especially in the urban areas of Nepal affecting 19% of population above the age of 40 years (Singh and Bhattarai, 2003). Diabetic retinopathy (DR), a most common complication of DM, is the leading cause of blindness among the working age people of developed world while more than 80% of its blinding sequelae occurs in low income setups (Report of WHO, 2005). DR is the fifth leading cause of global blindness, fourth leading cause of visual impairment contributing 4.8% of total blindness in the world despite being a preventable condition (Report of WHO, 2005).

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DR is an emerging eye health problem in the resource limited countries with increased trend of DM in such countries. Prompt laser therapy of vision threatening DR along with good glycaemic control and control of other concurrent risk factors reduces its blinding sequelae (Thapa et al 2012). Timely fundus evaluation and regular follow up of all stages of DR is essential to restore good visual acuity (ETDRS Research Group, 1981). In Nepal, there are estimated one million subjects having diabetes, three lacks diabetes subjects having DR and one lacks diabetes subjects having vision threatening diabetic retinopathy (VTDR). The VTDR are the subjects who need active intervention by the ophthalmologist. Despite some awareness, limited access for DR screening and limited vitreo-retinal services are the major barriers for service utilization in Nepal (Thapa et al, 2012, 2014). DR could be screened using various techniques such as direct and indirect ophthalmoscopy, and digital fundus photography (Moss et al, 1985; Diamond et al 1998; Saari et al 2004; Klein et al 1985; Lin et al 2002). There is further development in DR screening with the advancement in tele-ophthalmology and automated grading system (Perumalsamy et al 2007; Gupta et al 2013). Except few eye departments in government public hospitals, eye care service in Nepal is mainly provided by Non-governmental organizations. Allied Ophthalmic personnels (AOP) are often involved in fundus photography in many clinical setups besides their work in the district community eye centres (DCEC) in screening and treatment of simple ocular problems. Training to AOPs in detection of DR for referral of vision threatening retinopathy can help screen large volume of diabetes patients in a set up of low resource countries like Nepal with no Tele-Ophthalmology set up and adequate vitreo-retinal services.

This study aimed to assess the accuracy of DR grading using fundus photography by AOP as compared to ophthalmologist at a community DR screening program in Nepal.

Materials and methods

Fundus photographs of known DM attending for DR screening at district community eye centers and physician diabetic clinic of general public hospital of Nepal from June 2013 to December 2013 were enrolled in the study. The number of eyes for assessing the inter-rater agreement (between ophthalmologist and AOP) considering Kappa to detect (K = 0.80) with 90% power was at least 635 (Viera et al, 2005). However; in this study altogether 864 eyes of all subjects during the study period were enrolled. All fundus pictures were taken using Topcon digital fundus camera by the trained AOPs. One macula centered and one optic disc centered fundus pictures were taken before dilating the pupil. Five fundus pictures were taken under mydriasis. The mydriatic five fundus pictures were considered as the gold standard for DR grading. All the fundus pictures were graded by three ophthalmologist (vitreo-retina specialist) using 17-inch computer monitor and were considered as the best available standard as the comparator for agreement analysis. The same fundus pictures were graded by two types of AOP. The AOP 1 were the trained ophthalmic photographers who had completed government certified course to provide primary eye care in ophthalmology and were trained on DR grading. The AOP 2 were the eye health workers, who had received government certified course in medicine, then oriented on eye health care and then trained for DR screening using fundus photography and DR grading for at least six months. There were two persons in each group for DR grading among the AOPs and fundus photographs were graded using 17–inch computer monitor. DR was graded as per the Early Treatment Diabetic Retinopathy Study Criteria (ETDRS Research Group, 1981). Briefly; DR was broadly classified as non proliferative and proliferative DR. Non proliferative DR was further classified as mild, moderate, severe and very severe NPDR. Clinically significant macular edema (CSME) was defined as retinal edema located at or within 500 μm of the center of the macula

or hard exudates at or within 500 µm of the center if associated with thickening of adjacent retina or a zone of thickening larger than 1 disc area if located within 1 disc diameter of the center of the macula. Vision threatening retinopathy was categorized if subjects had severe NPDR, PDR or CSME at least in one eye. Before getting involved in the study, AOP were provided training in DR grading. The training conducted by retina specialist was based on detecting retinal findings of DR and grading severity of DR by interpreting several fundus photographs. Ophthalmologists involved in grading were the fellowship trained retina specialist. A special questionnaire to rate signs and severity of DR was designed with reference to some studies conducted on DR (Bryan et al, 2012; Thapa et al, 2016). Fifty fundus photographs were pretested for DR grading by all the graders and there was no problem while rating fundus photographs by the ophthalmologists and AOPs. The inter and intra rater agreement was assessed on yes or no answers on signs of DR on fundus photographs such as microaneurysm, retinal hemorrhages, exudates, neovascularization, tractional retinal detachment. The agreement on normal versus abnormal retina, normal versus abnormal macula, grading of mild, moderate, severe, very severe NPDR, PDR, CSME and vision threatening DR were also done. The level of agreement between ophthalmologist and AOPs were assessed using kappa coefficient (*k*). The agreement was less than chance if kappa was <0, slight agreement if kappa was 0.01-0.20, fair agreement if kappa was 0.21-0.40, moderate agreement if kappa was 0.41-0.60, substantial agreement if kappa was 0.61-0.80 and almost perfect agreement if kappa was 0.81-0.99 (Viera et al 2005). The study was approved by the Institutional Review Board and Ethics Committee of Tilganga Institute of Ophthalmology (TIO) and conducted in accordance with declaration of Helsinki.

Results

Fundus photographs of 864 eyes of 435 diabetic patients were evaluated in the study. Mean age of diabetes subjects who underwent for DR screening using fundus photographs was 53.2± 12.4 S.D. years and age ranged from 12 to 83 years. 18.9% of subjects had DR during grading of fundus photographs as gold standard. Majority had mild NPDR (7.5%) and moderate NPDR (5.6%) followed by 2.1% having severe NPDR and 1.2% PDR. CSME was found in 3.2% subjects.

There was substantial agreement in detection of normal versus abnormal macula [k; 95% confidence interval (CI)= 0.6 (0.6-0.7)] whereas agreement was moderate for hemorrhage [k; 95% CI= 0.6 (0.5-0.7)] and CSME by AOP 1. Similarly, the agreement was moderate for detection of normal versus abnormal fundus [k; 95% CI= 0.5 (0.4-0.5)], detection of exudates and CSME except retinal hemorrhage [k; 95% CI= 0.3 (0.3-0.4)] that had fair agreement for AOP2 as compared with ophthalmologist. Table 1

Table 1: Inter rater agreement between ophthalmologist Vs allied ophthalmic personnel on macular examination

Descriptions	Ophthalmologist Vs AOP 1		Ophthalmologist Vs AOP 2	
	Kappa	95% confidence interval	Kappa	95% confidence interval
Macula Normal Vs Abnormal	0.6	0.6-0.7	.5	0.4-0.5
Micro aneurysm	0.7	0.6-0.8	.5	0.4-0.5
Hemorrghage	0.6	0.5-0.7	0.3	0.3-0.4
Exudates within 500 micro meter of Foveal Centre	0.5	0.4-0.6	.5	0.4-0.6
Exudates more than 1 DD located within 500 micrometer of Foveal Centre	0.6	0.5-0.7	.6	0.4-0.7
Exudates in Other Sites	0.5	0.4-0.6	.5	0.3-0.6

Abbreviation: DD-disc diameter, AOP-allied ophthalmic personnel

The agreement as compared to ophthalmologist for AOP 1 was substantial for detection of normal versus abnormal retina [k; 95% CI= 0.7 (0.6-0.8)], and retinal hemorrhage [k; 95% CI= 0.7 (0.6-0.8)]. The agreement was moderate for detection of exudates [k; 95% CI= 0.5 (0.4-0.6)], venous beading [k; 95% CI= 0.6 (0.1- 1.0)], and tractional retinal detachment [k; 95% CI= 0.6 (0.1-1.0)] except in neovascularization [k; 95% CI= 0.7 (0.6-0.8)] that had fair agreement. Similarly, the agreement as compared to ophthalmologist for AOP 2 was substantial for detection of normal versus abnormal retina [k; 95% CI= 0.7(0.6-0.7)], hemorrhage [k; 95% CI= 0.6 (0.6-0.7)], exudates [k; 95% CI= 0.6 (0.5-0.7)], venous beading [k; 95% CI= 0.7 (0.2-1.0)]. There was slight agreement for detection of neovascularization [k; 95% CI= 0.2 (-0. 2- 0.6)]. Table 2

Table 2: Inter rater agreement between ophthalmologist Vs allied ophthalmic personnel on retinal examination

Descriptions	Ophthalmologist Vs AOP 1		Ophthalmologist Vs. AOP 2	
	Kappa	95% Confidence interval	Kappa	95% Confidence interval
Retina normal vs abnormal	0.7	0.6-0.8	0.7	0.6-0.7
Hemorrhage	0.7	0.6-0.8	0.6	0.6-0.7
Exudates	0.5	0.4-0.6	0.6	0.5-0.7
Venous beading	0.6	0.1-1.0	0.7	0.2-1
Neovascularization	0.2	0.2-0.6	0.2	0.1-0.3
Tractional RD	0.6	0.1-1.0	0.1	0.1-0.2

Abbreviation: RD-retinal detachment, AOP-allied ophthalmic personnel

The agreement on diagnosing no DR Vs presence of DR for AOP 1 as compared to ophthalmologist was moderate for single ([k; 95% CI= 0.6 (0.5-0.6)] and two fundus photographs [k; 95% CI= 0.6 (0.5-0.6)] whereas the agreement was substantial with mydrriatric five fundus photographs [k; 95% CI= 0.6 (0.6-0.7)]. Similarly, diagnosing vision threatening DR like PDR and CSME was substantial for single, two fundus pictures and mydriatric five fundus photographs. The agreement was ranged from fair to moderate for diagnosing other stages of NPDR by AOP 1. Table 3

Table 3: Inter rater agreements between ophthalmologist Vs allied ophthalmic personnel 1 on DR diagnosis in single, two and five fundus photographs

Patterns of DR	Single picture Kappa	95% Confidence interval	Two pictures Kappa	95% Confidence interval	Mydriatic five pictures (kappa)	95% Confidence interval
No DR	0.6	0.5-0.6	0.6	0.5 - 0.6	0.6	0.6 - 0.7
Mild NPDR	0.1	0.1-0.2	0.1	0.1 - 0.2	0.3	0.2 - 0.4
Moderate NPDR	0.4	0.3-0.5	0.4	0.3 - 0.5	0.4	0.3 - 0.5
Severe NPDR	0.4	0.2-0.5	0.4	0.2 - 0.6	0.4	0.2 - 0.5
Very S. NPDR	0.2	0.1-0.5	0.2	0.1 - 0.5	0.1	0.1 - 0.4
PDR	0.7	0.4-0.9	0.7	0.4 - 0.9	0.4	0.1 - 0.7
CSME	0.7	0.4-0.9	0.7	0.4 - 0.9	0.7	0.4 - 0.9

Abbreviation: DR-diabetic retinopathy, NPDR-non proliferative diabetic retinopathy, PDR-proliferative diabetic retinopathy, CSME-clinically significant diabetic retinopathy

The agreement on diagnosing no DR Vs presence of DR for AOP 2 as compared to ophthalmologist was substantial in non mydriatric single [k; 95% CI= 0.6(0.6-0.7] , two fundus photographs [k; 95% CI= 0.6 (0.6-0.6)] and mydriatric five fundus photographs [k; 95% CI= 0.6 (0.6-0.7)]. Similarly the agreement was substantial for diagnosing vision threatening DR; CSME. The agreement was ranged from fair to moderate for diagnosing other stages of NPDR and PDR by AOP2 Table 4.

Table 4: DR diagnosis between Ophthalmologist Vs MLOP 2 in non mydriatic single picture, two pictures and mydriatic five pictures

Patterns of DR	Single picture Kappa	95% Confidence interval	Two pictures Kappa	95% Confidence interval	Three pictures Kappa	95% Confidence interval
No DR	0.6	0.6 - 0.7	0.6	0.6 - 0.7	0.6	0.6 - 0.7
Mild NPDR	0.1	0.1 - 0.2	0.1	0.1 - 0.2	0.2	0.1 - 0.3
Moderate NPDR	0.4	0.3 - 0.6	0.4	0.3 - 0.5	0.4	0.3 - 0.5
Severe NPDR	0.3	0.1 - 0.4	0.3	0.1 - 0.4	0.3	0.1 - 0.4
Very S. NPDR	0.3	0.1 - 0.5	0.3	0.05 - 0.5	0.3	0.1 - 0.5
PDR	0.3	0.3 - 0.5	0.4	0.1 - 0.6	0.3	0.1 - 0.6
CSME	0.6	0.5 - 0.7	0.6	0.5 - 0.7	0.6	0.5 - 0.7

Abbreviation: DR-diabetic retinopathy, NPDR-non proliferative diabetic retinopathy, PDR-proliferative diabetic retinopathy, CSME-clinically significant diabetic retinopathy

Discussion

This is the first study to compare the agreement on DR grading between an ophthalmologist and AOPs using digital fundus photographs in a community setting in Nepal.

Except few eye departments, integrated eye care service is very minimal through the government sectors in Nepal. Most of the eye care services are provided through the NGO, INGO run eye hospitals and private medical colleges. Diabetic eye care service is not typically integrated in the comprehensive diabetes management. DCEC affiliated to one of the major tertiary level care hospital in each district are lead by the AOPs and provids basic eye care service, refraction, screening of diseases and referral of complicated eye problems to tertiary hospitals. So DCEC served as the first point of contact for the residence of that district. Further training to such cadres for DR screening could help early detection and referral of vision threatening DR cases for prompt treatment.

In this study, we trained two types of AOPs to screen DR using fundus photography and then to grade the fundus photographs for accuracy of DR. Good fundus photography technique is very important for accurately grade the pictures. The proportion of ungradable images is significantly high (30-50%) even in the better organized national screening programs, necessitating many persons to be referred for a comprehensive eye examination by an ophthalmologist. Adding training in retinal photography (image capture) is a value in diagnosis of referable pathology. In this study, the prevalence of DR was 18.7% while assessing fundus photographs and is almost similar to the studies of DR prevalence estimated on clinical examination (Paudyal et al, 2008; Shrestha et al; 2007). We stratified the AOPs in to two groups in this study. One group (AOP photographer) had prior expertise in retinal photography; the other groups were clinical personnel who did not have prior experience in image capture. Both groups received additional training in DR screening using fundus photography and grading of referable pathology as a part of this study.

In our study, there was substantial agreement in detection of normal versus abnormal macula by AOP1 and was moderate for AOP2. Similarly, there was substantial agreement with both AOP 1 and AOP2 for normal versus abnormal retina.

In a study conducted by Thapa et al, 2016 using mid level ophthalmic personnel for retinal diseases screening using fundus photography, the inter rater agreement for overall retinal pathologies was moderate. In this study, the agreement was better among those with more experienced in fundus photography (AOP1) and agreement was almost similar for AOP2.

In this study the agreement was moderate for macular hemorrhage, exudates (CSME) for AOP 1 where as it was fair to moderate for AOP2. This finding was also similar to the study by Thapa et al, 2016 where the agreement was moderate for detection of maculopathy.

Similarly, for retinal hemorrhage, there was substantial agreement for both AOP1 and AOP2. The findings are again similar to the previous series by Thapa et al, 2016. Retinal hemorrhages are the key signs of DR and for grading the severity. The better results for retinal hemorrhage is most likely due to its good visibility except in non gradable fundus pictures.

The agreement was moderate to substantial for detection of retinal exudates, venous beading for both AOP1 and AOP2 whereas the agreement was fair for neovascularization. There could be chance of missing early neovascularization even for the experienced ophthalmologist that needs further investigation with fundus fluorescein angiography for confirmation.

There was overall substantial agreement for diagnosing cases without DR and CSME in nonmydriatric single and two fundus photographs and mydriatric five fundus photographs. There was fair agreement for severe NPDR and PDR. The agreement was ranged from fair to moderate for diagnosing other stages of NPDR, and PDR.

There are no other similar studies conducted for DR agreement using these AOPs except in other cadres like primary care physicians (Farley et al, 2008).

DR screening has been advanced through tele-ophthalmlogy service to automated grading system in the developed world (Moss et al, 1985; Diamond et al, 1998; Saari et al, 2004; Klein et al, 1985; Lin et al, 2002). Despite these advances in the high income countries, in Nepal, awareness on DR, DR screening, referral and treatment service are still lacking far behind (Thapa et al, 2012; 2015). Further training to AOPs could also be utilized on counseling, DR screening and referral of vision threatening retinopathy. The finding of this study has also explored the possibility of training to allied medical personnel from physician diabetic clinic for sustainable comprehensive diabetes management, we recommend for such study in the future.

The limitation of the study is that we were not able to assess the intra-rater agreement between different graders in this study to assess the consistency on grading by the graders.

Conclusion

Allied ophthalmic personnel with training and resources could be a first level DR screener. Three out of five diabetics could be managed at community level and thus reduce workload of ophthalmologist at base hospital. They could be fairly accurate for action oriented sight threatening diabetic retinopathy screening rather than diabetic retinopathy screening. This modality of DR screening can be useful in other similar resource limited countries for early identification of vision threatening retinopathy to reduce diabetic retinopathy blindness.

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