Sensitivity and Specificity of Nonmydriatic Digital Imaging in Screening Diabetic Retinopathy in Indian Eyes

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Diabetic retinopathy (DR) constitutes sixth common cause of blindness in India. It is often asymptomatic in the early stage. Development of blindness is due to progression to an advanced stage of the disease. Most hospitals that treat diabetes don’t screen and treat DR. This is due to the lack of awareness both amongst the patients as well as treating physicians. The key to maintenance of good vision in these eyes is the early detection and treatment that can be done by screening all the patients with a diagnosis of diabetes mellitus (DM). Screening is vital not only to prevent visual loss but it is also a highly cost-effective health intervention programme.

The gold standard for evaluating DR is the seven standard stereoscopic 30 degrees field photographs. The non-mydriatic retinal imaging (NMRI) is being widely recommended for screening purposes in the West, but their sensitivity and specificity is not known in Indian eyes with dark brown irides. The present study evaluates the sensitivity and specificity of NMRI in screening DR in Indian eyes.

MATERIALS AND METHODS

Patients and Imaging

500 patients (1000 eyes) with type 1 or type 2 DM attending the endocrinology clinic were imaged between September 2008 and June 2010 and analyzed. Institute Ethics Committee approval was obtained. The exclusion criteria were:

1) History of previous laser treatment or vitreous surgery;
2) Patients who were already following up under a retina specialist;
3) Patients with significant physical or mental disabilities who were unable to sit at the camera or cooperate.
with photography; 4) Patients with significant cataract and corneal opacity in one or both eyes precluding fundus photography; 5) Patients not undergoing routine dilated fundus photography in the retina clinic after undergoing non-mydriatic imaging in the endocrinology clinic (because of absence of reference for grading DR).

The nonmydriatic fundus camera (Zeiss Procam) was stationed in the endocrinology clinic. A trained ophthalmic technician carried out the NMRI of the patients. Three 45 degree retinal field images were taken 1) Optic disc and macula, 2) Superotemporal to optic disc 3) Nasal to optic disc. This was followed by routine dilated fundus photography (Zeiss Visupac 450 plus fundus camera) in the Advanced Eye Centre.

**Grading of retinal images**

All six fundus images (both in color and red-free mode) from each eye were reviewed independently by two experienced retina specialists (VG, RB) and graded for quality of photograph (Higgs et al) and retinopathy.

Grade 1) Excellent.; Grade 2) Definition of most retinal detail clear; Grade 3) Definition limited, but most detail visible; minor degrees of retinopathy and fine disc or retinal new vessels might be missed; Grade 4) Only gross detail visible; larger hemorrhages and exudates may occasionally be detectable; Grade 5) No detail visible.

The DR was characterized as per Airlie House Classification of ETDRS. Any grade worse than mild NPDR was labeled as sight-threatening DR (STDR) to include all patients needing further investigations and medical interventions. These clinical levels were graded on dilated fundus photography and NMRI and then compared to evaluate the sensitivity and specificity of NMRI.

**RESULTS**

There were 306 males and 194 females. The mean age was 52.97 ± 13.46 years (range 9–84 years). Digital NMRI was analyzed by two masked observers (#1 and #2) and compared. The dilated fundus imaging was considered as the reference for detecting any form of DR. The rate of ungradable images was 30.6% and 31% by the two observers, respectively.

**Observer # 1:**

Of 500 patients, 153 (30.6%) patients had ungradeable images in at least one eye. In 347 (69.4%) patients, both eyes could be graded from undilated images. When analyzed in these 347 patients, the sensitivity of detecting any type of DR was 84.7%, Specificity 99.6%, PPV 98.9% and NPV 93.3%. The weighted kappa (κ) denoting the level of agreement between the undilated and dilated images was 0.876. However, since only 69.4% patients could be graded from undilated
images, the overall sensitivity, specificity, PPV and NPV in the screened population were reduced to 58.8%, 69.1%, 68.6% and 64.7%, respectively. The level of agreement was also reduced (κ = 0.608).

Observer # 2:

Of 500 patients, fundus of 345 (69%) patients could be assessed for presence or absence of DR in both eyes from undilated images. The sensitivity of detecting any type of DR was 83%, Specificity 99.1%, PPV 97.9% and NPV was 92.4%. The weighted kappa (κ) denoting the level of agreement between the undilated and the dilated images was 0.855. However, since only 69% patients could be graded from undilated images, the overall sensitivity, specificity, PPV and NPV in the screened population were reduced to 57.3%, 68.3%, 67.5% and 63.7% respectively. The level of agreement was also reduced (κ = 0.593). The level of agreement between the two observers was high (κ = 0.96).

DISCUSSION

Our results show a sensitivity of 84.7% and 83% by two independent observers for detecting any form of DR by the NMRI system. The accepted target for an effective screening programme is 80%. The sensitivity in our study decreases further if all patients with gradable and ungradable images are included. A very important aspect of designing and implementing a screening programme with NMRI is the rate of ungradable images. In our study, the rate of ungradable photos by NMRI is higher than that reported (12 to 25%) in many of the previous studies. Light irises have been shown to transmit more light than eyes with dark irises. The high pigment content blocks light from passing through the iris to the retina, restricting it to the pupil. The iris controls the amount of light that enters the eye. Bergamin et al studied the effect of iris color on pupillary light reflex in normal healthy volunteers and found that it significantly influenced the amplitude and velocity of pupillary contraction, but not the pupil size and latency time. A stronger pupillary light reflex in terms of increased, faster and prolonged pupillary contraction (as assessed by the amplitude, contraction velocity, and redilation velocity, respectively) was a significant finding in the brown iris group as compared to blue iris group in this study. Klein et al found that patients with brown irises were more discomforted by the flash than patients with blue irises. The NMRI without the use of dilators needs to be validated in Indian eyes before this technology can be used as a widespread screening tool for DR. A relatively lower sensitivity and a high rate of poor quality photographs pose major limitations in its usefulness as a perfect screening system, particularly in dark irides population with diabetes involving younger age groups as seen in Indian eyes.