Original Article

The Accuracy of Digital Imaging in Diagnosis of Retinopathy of Prematurity in Iran: A Pilot Study

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Abstract

Purpose: To evaluate sensitivity and specificity of digital retinal image reading in the diagnosis of referral-warranted retinopathy of prematurity (ROP).
Methods: Infants referred to the ROP clinic underwent fundus examination through indirect ophthalmoscopy. Fundus photographs were acquired using RetCam (shuttle 2; Clarity medical systems, Pleasanton, CA, USA). Four retinal specialists who were blind to patients' information reviewed the RetCam fundus photographs. By comparing the results of photographs' readings with that of indirect ophthalmoscopy as the gold standard, the sensitivity and specificity of telescreening was determined.
Results: A total of 147 treatment-naïve patients met the inclusion criteria and were enrolled in the study. Mean gestational age (GA) was 28.6 ± 2.0 weeks. Digital retinal imaging had sensitivity of 85% and specificity of 35% in detecting referral-warranted ROP in our study. Positive predictive value of digital photography was 80%, and negative predictive value was 43%.
Conclusion: Digital photography for diagnosis of ROP may show good potential as a screening modality in developing countries. It can facilitate early diagnosis, prevent unnecessary referrals, and be implemented for investigational purpose. However, the overall study result did not provide evidence to propose digital photography as a substitute for indirect ophthalmoscopy in the diagnosis of ROP.

Keywords: Ret Cam, ROP Digital Imaging; Telescreening

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INTRODUCTION

Retinopathy of prematurity (ROP) is one of the most common causes of childhood blindness worldwide.[1,2] Indirect ophthalmoscopy in the neonatal intensive care unit (NICU) is the standard screening tool for ROP.[3-5] This approach is effective in early detection of the vision threatening stages of the disease. However, it has significant limitations: need for ophthalmologists to travel to the NICUs, which is time consuming and costly; subjective documentation of clinical findings through hand drawing; and in controversial cases of PLUS disease, non-availability

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of the original fundus pictures for second opinion or future referral.

These limitations combined with the difficulty of neonatal ophthalmic examination have negatively impacted willingness of retinal specialists and pediatric ophthalmologists to be involved in the field.[6,7]

Telescreening has advantages of eliminating the necessity of ophthalmologists' travel to the NICU, documentation of clinical findings, sending images to ophthalmologists at remote location for consultation, improving early recognition of disease progression, cost-effectiveness, and hasvalue in education and research. Telescreening was reported to facilitate decision making and follow-up of ROP patients.[8,9]

Previous studies have reported the accuracy results of telescreening of ROP [Table 1]. In this study, we investigated the accuracy of digital imaging of ROP patients in a sample of Iranian neonates who were referred to the ROP clinic of our hospital.

METHODS

Neonates who were referred to the ROP clinic of Farabi Eye Hospital between March 2016 to November 2016 were included. This study was approved by the Institutional Review Board/Ethics Committee of the hospital. Informed consent was obtained from parents or guardians of all neonates before the study was initiated. The examinations were all in accordance with the guidelines provided by the World Medical Association Declaration of Helsinki on Ethical Principles for Medical Research Involving Humans. Neonates were excluded if any ocular media opacity or major ocular anomalies were present.

At first examination, all neonates underwent slit lamp biomicroscopy, and then mydriatic-cycloplegic eyedrops (combination of 0.05% tropicamide and 1% phenylephrine) were instilled twice in each eye about 45 minutes before indirect ophthalmoscopy. After attaining full dilation and cycloplegia, refraction was performed by an optometrist. Subsequently, one drop of 0.5% tetracaine was instilled in each eye followed by using a lid speculum. Indirect ophthalmoscopy with a 20-diopter condensing lens was performed by the ophthalmologist involved in the study to examine 360° of the retina up to the ora serrata with scleral depression. Presence or absence of ROP, staging of the disease, and presence or absence of PLUS disease were recorded per international classification of ROP.[9] Therapeutic plan was determined by two authors based on the clinical findings of indirect ophthalmoscopy and was documented on paper (patient's information sheet). Fundus photographs were acquired using RetCam (shuttle 2) (Clarity medical systems, Pleasanton, CA, USA) by experienced nurses of the ROP clinic.

Four retinal specialists, who were expert in the field and masked to the patients' information, reviewed the fundus photographs and recorded their individual judgment about the stage, zone of involvement, presence of PLUS disease, and need for treatment.

Referral-warranted ROP was defined as follows: zone I, any stage with PLUS disease; zone I, stage 3 without PLUS disease; and zone II, stage 2 or 3 with PLUS disease.

The results were analyzed to determine sensitivity, specificity, positive, and negative predictive values of the RetCam photographs in comparison to those of indirect ophthalmoscopy as the gold standard.

For statistical analysis, disease positive was defined for each eye as the presence of referral-warranted ROP diagnosed through indirect ophthalmoscopy, and test positive was defined as the presence of referral-warranted ROP detected through interpretation of RetCam photos.

Table 1. Accuracy results of telemedicine for detection of ROP in different studies

Study	Outcome measure	Sensitivity/ specificity
Present study	Referral-warranted ROP	0.85/0.35
Roth *et al*., 2001[17]	Any ROP	0.82/0.94
Dhaliwal *et al*., 2009[19]	Any ROP	0.60/0.91
Yen *et al*., 2002[20]	Any ROP at 32-34 GA	0.46/1.00
Chiang *et al*., 2006[16]	Any ROP	0.82-0.86/0.49-0.96
Ells *et al*., 2003[22]	Referral-warranted ROP	1.0/0.96
Shah *et al*. 2006[24]	Any ROP	0.86/0.92

RESULTS

A total of 147 treatment-naïve patients met the inclusion criteria and were enrolled in the study. Mean gestational age (GA) was 28.6 ± 2.0 weeks (range, 23-37 weeks) and mean birth weight was 1214 ± 29 grams (range, 700-2800 grams). Mean post-gestational age at first examination was 34.4 ± 3.8 weeks. Per indirect ophthalmoscopy findings, 204 eyes from 147 patients were diagnosed with PLUS disease and 221 eyes were referred for treatment including laser ablation, intravitreal bevacizumab injection, or surgery. Considering indirect ophthalmoscopy as the gold standard for ROP diagnosis, sensitivity and specificity of referral warranted cases and PLUS disease was calculated for each examiner and average value was calculated. Results are summarized in Tables 2 and 3. Digital photography reading showed mean sensitivity of 85% and mean specificity of 35% in detecting referral-warranted ROP in our study. Mean positive predictive value of digital photography was 80%, and mean negative predictive value was 43%.

Table 2. Accuracy result by each observer in detecting need for treatment in ROP

	Sensitivity	Specificity	Positive predictive value (95% Confidence interval)	Negative predictive value (95% Confidence interval)
Observer 1	0.59	0.61	0.82 (0.75-0.88)	0.33 (0.25-0.42)
Observer 2	0.95	0.22	0.78 (0.72-0.83)	0.65 (0.44-0.82)
Observer 3	0.96	0.22	0.79 (0.74-0.83)	0.64 (0.42-0.81)
Observer 4	0.86	0.36	0.80 (0.74-0.85)	0.47 (0.33-0.62)

Table 3. Accuracy results by each observer in diagnosis of patients with PLUS disease

	Sensitivity	Specificity	Positive predictive value (95% Confidence interval)	Negative predictive value (95% Confidence interval)
Observer 1	0.69	0.50	0.74 (0.64-0.81)	0.44 (0.31-0.57)
Observer 2	0.95	0.37	0.85 (0.79-0.89)	0.66 (0.44-0.83)
Observer 3	0.95	0.37	0.85 (0.79-0.89)	0.66 (0.44-0.83)
Observer 4	0.83	0.54	0.87 (0.80-0.93)	0.45 (0.29-0.62)

DISCUSSION

In this study, we evaluated the diagnostic accuracy of digital imaging in diagnosing referral-warranted ROP. The results indicated sensitivity of 85% and specificity of 35%.

Telemedicine is a recently emerged modality which has potential to improve management of ROP. It has benefit in developing countries where there is limited access to referral centers and retinal specialists who are experienced in ROP field. Digital imaging photo-documentation by trained nurses has been reported to cause less physiological stress to neonates than indirect ophthalmoscopy with scleral depression.[9]

Considering the low number of retina specialists who have expertise in the ROP field and wide geographic distribution of NICUs nationwide in Iran, digital telemedicine is an excellent alternative that can eliminate the need for transferring infants and allows consultation with specialists in remote centers. In addition, timely management of patients can be considered to prevent significant deleterious visual sequels.[10,11]

Some studies have evaluated accuracy of telemedicine for diagnosis of ROP. Of these, most considered dilated retinal examination as the gold standard. Regardless of the severity of disease, sensitivity and specificity of telescreening was 46-97% and 49-100%, respectively.[12-21] Table 3 summarizes the accuracy of telemedicine for detection of ROP in some previously reported studies.

Ells et al reported sensitivity of 100% and specificity of 96% for detection of referral-warranted ROP.[22] Wu et al reported sensitivity of 100% and specificity of 98% for detection of prethreshold disease.[23] Roth et al evaluated accuracy of the RetCam system for detecting various stages of ROP in older infants and reported sensitivity of 82% and specificity of 94%.[17] In patients with lower postnatal age and milder ROP disease, the accuracy was lower compared to that in the other groups.[20]

Digital photography has added advantage of the possibility of comparing serial photographic examinations for therapeutic and research purposes. This is valuable considering that hand drawings have great variability even among experts.[23,24]

With regard to accuracy of digital photography, various studies have proposed it as an excellent screening modality for ROP in developing countries.[12-20] However, our study did not support this method as a substitute for indirect ophthalmoscopy.

In summary, considering the large number of ROP patients to be screend, telescreen digital photography can improve the management of patients, prevent significant deleterious visual sequels, and facilitate research. However, based on the results of the study, digital imaging cannot be proposed as a substitute for indirect ophthalmoscopy; further study including more patients and graders is required.

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Conflicts of Interest

There are no conflicts of interest.

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