# Identification of risk factors and evaluation of digital funduscopic screening for retinopathy of prematurity in a regional neonatal unit in Australia

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(Key words: Retinopathy of prematurity, risk factor, digital funduscopic screening)

**Abstract**

***Objectives:*** To identify risk factors significantly associated with retinopathy of prematurity (ROP) and evaluate the usefulness of digital funduscopy for ROP screening in a regional neonatal unit in Townsville, Australia.

***Method:*** This is a retrospective study. Basic data was retrieved from the department's prospectively maintained database and stored in the digital camera (Retcam) data storage device. ROP candidates were defined as babies who were born with a birth weight at or less than 1250 g and/or, born at or before 28 weeks.

***Results:*** One hundred babies satisfied the criteria for inclusion into the study. There were 44 male neonates. Birth weights ranged from 470-1342g (mean 986±177). Female babies were significantly smaller than males ($p<0.05$). Mean gestation at age was 27.2±1.9 weeks. There was no significant difference in gestational age of male and female babies ($p>0.05$). Twenty three babies had ROP. Retinal images from 6 babies were sent for remote expert opinion and 2 babies were transferred for treatment.

***Conclusions:*** ROP is significantly associated with prematurity. More clinical trials on bigger cohorts are necessary to evaluate digital funduscopy on ROP screening.

**Introduction**

Retinopathy of prematurity (ROP) is a retinal vascular disorder in premature infants and a leading cause of childhood blindness throughout the world[1]. It was first noticed in the 1940s when more and more oxygen was being administered to premature infants[2]. This disorder was called retrolental fibroplasia by Terry in 1941[2]. The term retinopathy of prematurity was coined by Heath in 1951[2]. Although the incidence and severity of ROP have been decreasing in developed countries over the past two decades, they are showing an increase in developing nations[3].

The standard method of diagnosis of ROP has been bedside indirect ophthalmoscopy for both routine clinical care as well as clinical trials[4]. However, indirect ophthalmoscopic screening has its limitations[4]. Indirect ophthalmoscopy examinations are labour intensive for the ophthalmologist and potentially stressful for patients[5]. The examiner's interpretations of the clinical findings, rather than the actual retinal features, are transcribed on to grading sheets[4].

Retinal photography to evaluate ROP was described nearly 4 decades ago[6]. Store and forward telemedicine is an emerging technology that involves the capture of patients' data for subsequent interpretation by a remote medical specialist[7]. There is significant interest in the use of retinal imaging devices for ROP screening[4]. RetCam (Clarity medical systems) is a wide angle camera which provides a greater view of retina (eg $130^0$ field of view) which can produce digital retinal images which could be transferred remotely for evaluation.

There are advantages and disadvantages of both types of examinations[5]. Advantages of indirect ophthalmoscopy include more complete documentation of ROP and usually better visualization of the fundus by the ophthalmologist; disadvantages include availability and time constraints of the ophthalmologist[5]. RetCam screening may be advantageous in that it may be performed by a technician or nurse with possibly more flexibility in scheduling, although disadvantages include limitation of image quality and complete detection of ROP[5]. Another disadvantage of RetCam screening includes the initial cost of the equipment, although over time this may be balanced by decreased costs of ophthalmology referrals[5].

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**Objectives**

- To identify the risk factors significantly associated with ROP.
- To evaluate the usefulness of digital funduscopy for ROP screening in a regional neonatal unit in Townsville, Australia.

**Patients and methods**

The study was carried out in the neonatal unit of the Townsville Hospital, Queensland, Australia. The neonatal unit has 12 neonatal intensive care unit (NICU) cots and 20 special care cots and looks after 700 sick babies per year from North Queensland. Eye examination for ROP is done as a bedside procedure by two specialist ophthalmologists who visit the unit on a roster basis. Until the beginning of 2007, all examinations were carried out by indirect ophthalmoscopy. Since early January 2007 all ROP candidates in the unit were examined using Ret Cam II Wide Field Digital Imaging System (Clarity Medical System, Pleasanton, CA 94588, USA).

All ROP candidates born between January 2007 and June 2009 and admitted to our NICU who have been examined by using the RetCam II in the unit were enrolled in the study. Ethical clearance was obtained from the Ethical Committee of The Townsville Health District. We define ROP candidates in this study as babies born with a birth weight of ≤1250g and/or, born ≤ 28 weeks or both. These are modified guidelines formulated by the local ophthalmologists at The Townsville Hospital as only 2 ophthalmologists are available.

During the study period all the eye examinations were carried out using RetCam II (Digital retinal imaging) by 2 ophthalmologists who visit the unit on a roster basis. First eye check was carried out on each of the babies at a corrected age of 32 weeks. Subsequent examinations were scheduled biweekly if no ROP was present and weekly if ROP was present. Screening was continued until the infant was discharged or transferred from the unit or until the retinal vasculature was mature. All eye examinations were carried out after dilatation with 0.5% cyclopentolate. Retinal images were analysed and stored in RetCam for further evaluation when necessary. Babies who need cryotherapy or laser therapy were referred to the Paediatric Ophthalmologist at the Royal Children's Hospital (RCH) in Brisbane.

This was a retrospective study. Basic data was retrieved from department's prospectively maintained database and the data stored in the RetCam data storage device. Demographic and clinical data were collected on all infants including birth weight, gestational age, gender, ethnicity, Apgar scores and number of hours exposed to oxygen. Results of ophthalmic reviews for ROP and outcome were separately analysed. Student's t test and Chi-square tests were used where appropriate and p value of $< 0.05$ was accepted as significant. Statistical analysis was carried out using Stata Intercooled Ver. 9.0, StatCorp, Texas, USA.

**Results**

A total of 100 patients were analysed. There were 44 males and 56 females. The birth weights ranged from 470 - 1342 g (mean 986± 177). Female babies were significantly smaller when compared to male babies. (955 g and 1025 g respectively, $p = 0.0494$; $p<0.05$).

The mean gestation at age was 27.2 ± 1.9 weeks (range 23 to 33 weeks). There was no significant difference in gestational age of male (27.3 weeks) and female babies (27.9 weeks) ($p = 0.14$; $p>0.05$)

Twenty three (23%) babies had ROP and table 1 shows the different stages of ROP in these patients. There was no significant difference in the presence of ROP between male and female babies ($p = 0.67$; $p>0.05$).

**Table 1**
**Different stages of ROP in the cohort.**

| ROP Stage | Number of patients |
|---|---|
| 1 | 9 |
| 2 | 12 |
| 3 | 2 |

The median duration of exposure to added oxygen was 322 hours. Logistic regression modelling showed that the likelihood of developing ROP was significantly related to gestational age. Table 2 shows the relationship between the available variables with the likelihood of developing ROP.

**Table 2**
**Odds ratio of the risk factors on development of retinopathy of prematurity**

| Variable | Odds ratio | P value | 95% CI |
|---|---|---|---|
| Birth weight (g) | 1.000 | 0.629 | 0.99 -1.01 |
| Gestation | 0.514 | 0.018 | 0.30 -0.89 |
| Hours needing oxygen | 1.000 | 0.154 | 0.99 -1.00 |
| Sex | 0.807 | 0.708 | 0.26 -2.48 |

## Discussion

The Royal College of Paediatrics and Child Health, United Kingdom in their guideline states that all babies less than 32 weeks gestational age or less than 1501g birth weight should be screened for ROP[8]. However, in our study we only screened babies who were born with a birth weight at or less than 1250g and/or, born at or before 28 weeks of gestation. This was because the local ophthalmologists modified the guideline to reduce the workload.

During our study period we referred images from 6 babies for expert opinion. Two babies needed to be transferred for treatment. We found this a better option than transferring sick premature babies as it saves transfer costs, and more importantly, alleviates the complications associated with transferring sick infants for expert eye examinations.

The incidence of ROP is increasing globally. In developed countries the number of infants at risk for ROP is rising because of increasing premature birth rates resulting from assisted conception, increasing maternal age, socioeconomic factors, and possible genetic causes[9,10]. In Asia, Latin America, and Eastern Europe, the number of ROP cases has increased because of higher overall birth rates, as well as improved neonatal survival resulting from greater availability of neonatal care[11,12].

Manpower issues, costs associated with repeated transport of infants to remote tertiary centres for periodic ophthalmic surveillance and the spectrum of significant medico-legal liability associated with ROP are but a few of the barriers to achieving the goal of universal screening[13]. Use of digital funduscopy (telemedicine) for ROP screening appears to alleviate these problems to a certain extent. Yet, evidence based studies comparing the outcomes and process of digital screening to screening with indirect ophthalmoscopy are critical before widespread acceptance of the digital fundoscopic approach[13]. Blood vessels in the retina can be directly visualised non-invasively in vivo. The availability of digital photography and the technology to store, retrieve and transmit this data has made this an important clinical tool. The value of this imaging technique is further enhanced by the availability of software to carry out automated analysis.

The main limitation of this study is that it is not a randomised controlled trial. This is a retrospective audit looking at the number of patients who had their ROP assessment done using the RetCam technology. We found that there is a significant relationship between low gestational age and ROP. Even though low birth weight has been proven to be a major risk factor for ROP[7], this was not the case in our study. There was no significant association between number of hours exposed to oxygen and degree of severity of ROP. It would have been more useful to look at the number of hours in conjunction with concentration of oxygen rather than the duration of exposure only.

## Conclusions

- There is a significant association between prematurity and increased incidence of ROP.
- For the analysis of risk factors it is more appropriate to study a bigger cohort.
- Though digital imaging seems to have lot of advantages over indirect ophthalmoscpoy for ROP screening it is essential to have more evidence by means of comparative studies regarding accuracy, cost effectiveness, side effects and disadvantages.

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