Incidence of retinopathy of prematurity in Christchurch Hospital, New Zealand over a 10-year period

Louis S Han, Antony Bedggood

ABSTRACT

AIM: To describe the incidence of retinopathy of prematurity (ROP) in the Christchurch Hospital neonatal intensive care unit over a 10-year period.

METHOD: All neonates included in ROP screening from 2007–2016 were identified. Patient demographics and clinical details including the gestational age at birth, birth weight, birthplace, stage of ROP and treatment status were collected for analysis.

RESULTS: Over 10 years, 431 eligible babies born in Christchurch Hospital and admitted to NICU were examined and had findings documented. Nineteen were found to have ROP of any grade, and three required treatment. One hundred and thirteen neonates born outside of Christchurch and later admitted to the Christchurch NICU had screening examinations documented. Eighteen of these were diagnosed as having ROP, and eight required treatment. Five of the neonates born outside Christchurch who required treatment had been specifically transferred to Christchurch for the purpose of treating ROP.

CONCLUSION: The incidence of retinopathy of prematurity of any stage was 4.4% in at-risk premature neonates born in Christchurch Hospital over 10 years. 0.7% of all neonates screened required treatment. This represents an extremely low incidence of treatment requiring ROP, and of ROP in general.

Retinopathy of prematurity (ROP) is a potentially blinding disease associated with early exposure to high levels of oxygen in neonates. The relative hyperoxic state leads to cessation of normal retinal vessel growth, endothelial cell death, ischaemia, increased VEGF production and finally, retinal neovascularisation. Screening for the clinical signs that accompany these changes in ‘at risk’ infants is the cornerstone of ROP management. Timely detection and treatment is crucial to avoid poor structural and functional visual outcomes. ROP remains one of the leading causes of childhood blindness.

The current New Zealand guidelines indicate that screening for ROP is required in all babies who are less than 1,250g birth weight, <30 weeks gestational age (GA), or in selected infants with an unstable clinical course who are believed to be at high risk by the attending neonatologist. Australasian data indicates 33% of neonates screened accordingly will have ROP of any severity. Previous international guidelines produced by the American Academy of Pediatrics suggested screening those born earlier than 32 weeks gestation, or weighing less than 1,500g. It is now accepted that extremely few babies born over 1,250g or 30 weeks develop treatment requiring ROP.

Christchurch Hospital is a tertiary New Zealand hospital serving a population of 510,000 from the wider Canterbury region for neonatal care. The Neonatal Intensive Care Unit (NICU) is a Level 3 facility with 10 intensive care cots and 28 Level 2 cots. It also provides care for all neonates requiring treatment of ROP in the South Island, (population of approximately one million) except...
the Nelson region (population 50,000) where ROP treatment is provided by another, closer tertiary centre.

As is the case in all South Island centres, ROP screening in Christchurch was performed by a comprehensive ophthalmologist using indirect ophthalmoscopy during the period of this audit. The Christchurch NICU changed its screening criteria to only include those less than 30 weeks or 1,250g in 2015. Prior to this any neonate under 1,500g, or less than 32 weeks GA was eligible for screening, but only those deemed to be at risk by their neonatologist were screened.

In the Christchurch neonatal unit, initial screening is performed at 30–31 weeks GA for those born younger than 26 weeks GA, or four weeks after birth for those older than 26 weeks GA at birth. Examination is repeated every two weeks until term, or as often as needed when more frequent assessment or treatment is required. ROP status is recorded according to zone, stage and the presence of plus or pre-plus disease as per the International Classification of ROP (ICROP).

**Method**

Data was collected and managed in two subsets, covering 2007–2014 and 2015–2016 respectively, as the screening criteria changed in 2015 in the Christchurch NICU. These were termed Period 1 and 2 in the results.

Neonates at risk of ROP were identified from two sources of hospital data. The first source was an internal NICU dataset, which was searched to identify all neonates eligible for ROP screening according to the criteria in place at that time. All patients coded as being diagnosed with retinopathy of prematurity in this group were identified. The stage of ROP and any treatment undertaken was determined when more frequent assessment or treatment is required. ROP status is recorded according to zone, stage and the presence of plus or pre-plus disease as per the International Classification of ROP (ICROP).

The second method employed utilised the Christchurch Hospital patient data system, searching for patients equal to or younger than six months of age at the time of discharge, with a coded diagnosis of retinopathy of prematurity. The coding used was H35.1 from the 10th revision of the International Classification of Disease (ICD-10). A search was also taken using procedural codes—4280900 and 4280901—destruction of retina by photocoagulation, and repair of retina by photocoagulation. The search was for infants less than six months old between January 2007 and December 2016 inclusive.

The two sets of results, cross-referenced with the hospital intranet system, were used to identify all of those who had ROP diagnosed during their stay. Patient demographics including birthplace, gestational age at birth and birthweight were recorded, as was the worst stage of ROP identified, and whether they received treatment.

In addition, a final check was used to ensure the validity of treatment data. All 532nm frequency doubled neodymium-doped yttrium aluminium garnet (Nd-YAG) laser use in the operating theatre is recorded. This laser logbook was searched to find the number of neonates who had retinal photocoagulation for ROP over the 10-year period. This matched exactly the number of treated neonates we had identified electronically.

This audit was performed in the tenets of the declaration of Helsinki and the New Zealand National Ethics Advisory Committee guidelines. It was exempt from formal Health and Disability Ethics Committee review.

**Results**

During Period 1, from January 2007 to December 2014, a total of 704 babies younger than 32 weeks gestational age were admitted to Christchurch Neonatal Intensive Care Unit. Of the 704 admitted, 460 (65%) babies were screened for ROP and had findings documented. During this period, there were only 26 documented cases of retinopathy of prematurity of any severity, and five neonates required treatment. Three hundred and fifty-six of the screened babies had been born in Christchurch Hospital, and of this group there were 14 affected by ROP, with only one requiring treatment. There were 104 babies screened for ROP who were born outside Christchurch Hospital; of this group 12 were diagnosed with ROP, and four required treatment.

During Period 2, from January 2015 to December 2016, 101 babies younger than 30 weeks gestational age were admitted to NICU, 84 (83%) neonates were examined and had findings documented. ROP of any stage was diagnosed in 11, six of whom were treated. Subgroup analysis shows
that 75 of the 84 screened had been born in Christchurch Hospital, five of whom were diagnosed with ROP, and two treated for ROP. Nine babies examined during this period had been born outside Christchurch, six of these had a diagnosis of ROP, and four required treatment.

One baby was identified through the clinical coding method but was not captured in the NICU data. They were born outside Christchurch, having been transferred from another level 3 NICU for treatment of ROP at 36 weeks GA. They were included in our analysis.

As seen in Table 1, over this 10-year period 431 neonates born in Christchurch Hospital were screened for ROP. Nineteen of them were diagnosed with ROP, and three required treatment. This represents an ROP incidence of 4.5% (19/431) for neonates born in Christchurch, and a 16% (3/19) incidence of treatment requiring disease, or 0.7% (3/431) incidence for all infants screened.

A total of 113 neonates born outside Christchurch Hospital were screened for ROP at Christchurch NICU. Eighteen were found to have ROP, with eight requiring treatment. Of those treated, five had been transferred to Christchurch for the purpose of assessment and treatment of ROP. The incidence in this group is 16% (18/113), 44% (8/18) of whom required treatment.

Median gestational age at birth and birthweight were also recorded for those diagnosed with ROP, the results are in the table below. Median GA for those diagnosed with ROP was 25 weeks, ranging from 23 to 30 weeks, with median birth-weight being 725 grams (range: 510–1,400g).

### Discussion

It is likely that there are very low rates of treatment requiring retinopathy of prematurity in New Zealand, especially when compared with overseas data. A large study in the UK found that 4% of live births weighing less than 1,500g were treated for ROP. The incidence of treatment requiring ROP in what should be relatively similar populations and neonatal care reported in Australian metropolitan centres, during a similar time period to our study, has been reported to be seven times greater than what is found in our results.
A review by Tan et al of all New Zealand neonatal units over the period of 2005–12 indicated 2% of very preterm infants (≤31 weeks’ gestation) were treated for ROP.11 0.7% of Christchurch-born premature neonates required treatment, with a median birth weight of 940gm and gestational age of 25 weeks. The incidence of treatment requiring ROP in Christchurch-born premature neonates 2007 to 2014 was extremely low, at 0.2%.

There has been a relative decrease in the incidence of ROP in Western countries since the findings of the CRYO-ROP study.2 The overall incidence for infants whose birth weight was <1,251gm was 65.8% in CRYO-ROP. Studies in the late 20th century found 34% developed any ROP in those with birth-weight less than 1,251g.12

Eighteen percent of infants <1,251gm developed stage 3 or worse ROP in CRYO-ROP, and 6% reached ‘Threshold’ disease requiring treatment.3 The incidence of severe ROP (stage 3 or 4) in New Zealand in those with birth-weight under 1,000 grams was reported to be 10.4% in 2006.13

Our audit shows that during a 10-year period, between 2007 and 2016, only 3% of neonates eligible for ROP screening who were admitted to Christchurch NICU after being born in Christchurch Hospital were diagnosed as having any retinopathy of prematurity. This represents at least a three-fold lower incidence of developing ROP for infants born in Christchurch and admitted to NICU, when compared with data from Australasia as a whole.6

When the two sets of data from 2007–2014 and 2015–2016 are compared, we find that the observed incidence of any ROP doubles from 3.9 to 6.7% and the number requiring treatment is ten times the rate in the previous eight years, 0.28 to 2.7%. The number being treated in this latter group represents a more ‘normal’ rate when compared to the national, Australasian and recent UK data.6,9,13

Table 2: Gestational age and weight at birth of patients with ROP, and the subgroup by birthplace.

<table>
<thead>
<tr>
<th>All patients with ROP†</th>
<th>Patients with any ROP (n=37)</th>
<th>Severe ROP‡ (n=11)</th>
<th>Not severe ROP (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median GA</strong> in weeks at birth (IQR)§</td>
<td>25 (24–26)</td>
<td>25 (23.5–25)</td>
<td>25 (24–27)</td>
</tr>
<tr>
<td><strong>Median birthweight in grams (IQR)</strong></td>
<td>725 (680–950)</td>
<td>750 (562.5–880)</td>
<td>832.5 (680–957.5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Christchurch Hospital born</th>
<th>Any ROP (n=19)</th>
<th>Severe ROP (n=3)</th>
<th>Not severe ROP (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median GA</strong> in weeks at birth (IQR)§</td>
<td>25 (25–27.5)</td>
<td>25 (Range 24–30)§</td>
<td>25.5 (25–27)</td>
</tr>
<tr>
<td><strong>Median birthweight in grams (IQR)</strong></td>
<td>920 (680–990)</td>
<td>940 (Range 760–1,060)</td>
<td>910 (680–957.5)</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Born outside Christchurch Hospital</th>
<th>Any ROP (n=18)</th>
<th>Severe ROP (n=8)</th>
<th>Not severe ROP (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median GA</strong> in weeks at birth (IQR)§</td>
<td>24.5 (24–25.5)</td>
<td>24.5 (23.5–25)</td>
<td>24.5 (24–26)</td>
</tr>
<tr>
<td><strong>Median birthweight in grams (IQR)</strong></td>
<td>737.5 (622–817.5)</td>
<td>722.5 (562.5–775)</td>
<td>765 (698–945)</td>
</tr>
</tbody>
</table>

†ROP, retinopathy of prematurity.
‡Severe ROP indicates treatment requiring ROP.
§GA, gestational age; IQR, interquartile range.
§Range given as total number in this group is three.
The very low incidence of ROP and ROP requiring treatment in Christchurch between 2007 and 2014 could be due to a large number of factors, most importantly the local NICU protocols, such as those determining target Sp02. Christchurch neonatal unit target saturations were 88–92% during the period of 2007–14, and 90–94% from 2015. This change was made based on the findings from a multinational randomised controlled trial looking at oxygen saturation and outcomes in preterm infants. This study showed that lower saturation targets were associated with higher mortality, but also a reduced rate of treatment for retinopathy of prematurity.\textsuperscript{14} The findings from our audit appear to be consistent with this, with a very low rate of ROP during the period of low target Sp02, increasing to a more ‘normal’ level once this target had been raised.

Variations in survival rates of extremely premature infants can potentially affect ROP incidence. If there are proportionally lower numbers of surviving higher-risk neonates, the incidence of ROP will also be lower. Firstly, there was a mild reduction in survival at 24 weeks gestational age at birth for premature infants born in Christchurch, when compared to other Australian and New Zealand neonatal networks over the period studied. Also, infants born at 23 weeks GA are likely to be under-represented in our study due to local policies regarding viability. Secondly, mortality rates for twins have been higher in Christchurch compared to other Australasian centres. Lastly, there was a period where antenatal steroid treatment given was later deemed to have been inadequate, and therefore subsequent respiratory function and other factors may have differed from other centres. (Associate professor N Austin, Department of Paediatrics, University of Otago. 2018, oral communication, 4th May.)

Patient demographics in Christchurch, including ethnicity, socioeconomic status, and maternal age may have been different to those found in other centres. It is likely that the population changed during the time of our study, especially with major Christchurch earthquakes in 2010 and 2011. Other key variables could include the percentage of multiple pregnancies, and of medical assistance, both being associated with ROP.

There has been a shift to promote breastfeeding in all babies. In 2014, Christchurch opened New Zealand’s first Human Pasteurised Donor Milk Bank. The incidence of ROP appears to vary with use of breast milk in premature infants. In a study by Manzoni et al comparing 314 exclusively breast-fed infants to 184 formula-fed preterm infants, there was significantly lower incidence of ROP of any severity and ‘threshold disease’ as defined in ETROP study, in the breastfeeding group.\textsuperscript{15} This could possibly influence the incidence seen in Christchurch.

We have assumed that prior to 2015 the 35% of potentially eligible neonates who were not screened were those who were older or heavier and therefore not at risk. During this period there were two neonates of 30 weeks gestational age at birth who were found to have any ROP. Both of them were less than 1,251gm and would have been captured in the new screening criteria. One of the two had ROP that required treatment.

We have also assumed that all neonates developing any ROP were identified. Sixteen percent of the neonates diagnosed with any ROP in the Christchurch-born group required treatment, which is consistent with the results from other studies.\textsuperscript{16} It is possible that there are cases who were not diagnosed, or which were not included in our data due to transfer to another NICU, or loss to follow-up. We are aware of one neonate not found to have any ROP when screened until 36 weeks of gestational age who went on to develop advanced bilateral disease after transfer and loss to follow-up. The numbers of infants involved is very small, but even a single case transferred out of Christchurch which required treatment, or any having a missed diagnosis, could significantly alter the findings.

During the period studied there were eight neonates born outside of Christchurch who required treatment for ROP, more than double the number in Christchurch-born neonates. Most of these were transferred from another NICU once the diagnosis of treatment-requiring ROP had been made. Many of the other neonates would have been transferred to Christchurch for the purpose of paediatric surgery and other medical treatments available at this tertiary
centre. Thus, the higher rate of both ROP and treatment in this group reflects a subset who were smaller, younger and generally more unwell, as well as those who had already been diagnosed as having advanced ROP.

It is interesting to note that 36% (4/11) of the neonates treated for ROP in Christchurch from 2007–2016 required re-treatment. This is higher than what is quoted elsewhere in the literature, but the numbers are too small to draw any useful conclusions. The characteristics of these patients are shown in the Table 3.

Two countries with an ROP registry were found during literature searches. Germany has a register with nine centres participating, which provides information on the demographics, incidence rate of severe ROP, stages of ROP, treatment, recurrence and other complications. Sweden has a nationwide register (SWEDROP) which was initiated in 2006, with national coverage of 96%. It is updated at every examination, and occurs for those infants that have been transferred to a different department. It has been used to study the epidemiology of ROP in Sweden, as well as enabling “tracking” of the infants at risk.

Our audit has its limitations. It is a retrospective study, which can lead to poorer quality of data when compared to a prospective study. There may have been patients with retinopathy missed in the data collection (ie, not recorded) as we relied on clinical coding and the neonatal unit’s internal data. The method of screening and who undertakes screening is a potential source to explain some local variation in incidence. A move to wide-field digital fundus imaging for neonates at risk of developing ROP could improve accuracy of diagnosis and facilitate effective follow-up and data collection.

Once we have established wide-field digital fundus imaging we intend to re-assess the prevalence of ROP in infants born and screened in Christchurch NICU. Sp02 control remains the same now as it was in the neonates screened from 2014–2016, as do screening criteria and other potential factors such as expressed breast milk banking and presumably demographics. If a consistently low ROP prevalence can be confirmed, then further research regarding the potential ROP influencing factors discussed can be undertaken.

A shift to recording of data that is not susceptible to transposing errors or data loss is also planned. We suggest establishment of a nation-wide electronic system to allow staging and diagnosis to be tracked. This could make clerical, recording and referral/data transfer between NICUs less susceptible to human error or lapses in communication between specialists or NICUs.

Table 3: Characteristics of patients that have been treated for ROP, and those that had repeat treatment.

<table>
<thead>
<tr>
<th></th>
<th>All patients treated for ROP† (n=11)</th>
<th>Patients that had single treatment (n=7)</th>
<th>Patients that had repeat treatment (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median GA‡ in weeks at birth (range)</td>
<td>25 (23–30)</td>
<td>25 (24–30)</td>
<td>23.5 (23–25)</td>
</tr>
<tr>
<td>Median birthweight in grams (range)</td>
<td>750 (510–1,060)</td>
<td>760 (530–1,060)</td>
<td>660 (510–940)</td>
</tr>
<tr>
<td>Median GA at first treatment (range)</td>
<td>37 (34–40)</td>
<td>37 (34–38)</td>
<td>37.5 (36–40)</td>
</tr>
<tr>
<td>Median GA at repeat treatment (range)</td>
<td>Not applicable</td>
<td>N/A</td>
<td>41 (36–44)</td>
</tr>
</tbody>
</table>

†ROP, retinopathy of prematurity.
‡GA, gestational age.

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**Competing interests:**
Nil.

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