An evaluation of the screening for retinopathy of prematurity in very-low-birth-weight babies at a tertiary hospital in Johannesburg, South Africa

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Background. Retinopathy of prematurity (ROP) is a leading cause of blindness for very-low-birth-weight (VLBW, <1 500 g) babies. ROP screening identifies babies that require treatment to prevent major visual impairment.

Objectives. To evaluate the screening for ROP at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) by reviewing the number of babies screened according to the CMJAH guidelines, the grades of ROP found and the treatment modality received.

Methods. This was a retrospective record review of VLBW babies born between 1 January 2013 and 31 December 2013 at CMJAH, whether inborn or transferred in. The babies were divided into two groups based on age at final outcome. Final outcome was defined as death, discharge or transfer out of the unit. The ‘early’ outcome group had their final outcome before day 28 of life. The ‘late’ outcome group had their final outcome at day 28 or more of life. The early outcome group qualified for outpatient ROP screening and the late outcome group qualified for inpatient ROP screening.

Results. There were a total of 572 VLBW babies at CMJAH during this time period. The babies had a mean birth weight of 1 127 (standard deviation [SD] 244.75) g and gestational age of 29 (2.743) weeks. The mean duration of stay was 29 (21.66) days and there were 309 female babies. Of these 572 babies, 304 comprised the early outcome group and 268 comprised the late outcome group. In the early outcome group babies who were transferred out of the unit or died were excluded; therefore, the remaining 147 babies discharged home qualified for outpatient ROP screening. Inpatient ROP screening was carried out in 36/147 (24.4%) of these babies (not in accordance with ROP screening guidelines). ROP was documented in 4/36 (11.1%). Outpatient ROP screening records were unavailable. Exclusions from the late outcome group included five babies. In the late outcome group 111/263 (42.2%) were screened for ROP. ROP was found in 17%. One baby required treatment with intravitreal antivascular endothelial growth factor (VEGF) and three babies required surgery.

Conclusions. More than half of the babies in the late outcome group were not screened during their stay (57.8%). More than one-third of babies were discharged prior to reaching the current recommended age for screening. Efforts need to be intensified to identify and screen all eligible babies prior to discharge. Outpatient ROP screening is not well documented; therefore, prevalence cannot be established.

VLBW babies at 4 - 6 weeks chronological age

The SAMJ guidelines recommend screening all to capture images of the retina. The 2013 techniques involve the use of digital cameras indirect ophthalmoscopy. Newer screening out by an ophthalmologist and by means of

where the risk of a serious adverse outcome is reached a stage where the risk of a serious adverse outcome is considered minimal. ROP screening is carried out by an ophthalmologist and by means of indirect ophthalmoscopy. Newer screening techniques involve the use of digital cameras to capture images of the retina. The 2013 SAMJ guidelines recommend screening all VLBW babies at 4 - 6 weeks chronological age or 31 - 33 weeks corrected GA – whichever comes last. The guidelines detail where and how to screen, as well as how to follow up and manage patients and when to stop screening. These guidelines are in line with the WHO Vision 2020 strategy. Vision 2020 ensures the availability of ophthalmologists experienced in indirect ophthalmoscopy who can identify premature babies who require treatment for ROP, that babies at risk for ROP have their fundi examined starting 4 - 6 weeks after birth, and that those with severe disease are treated immediately.

ROP is classified according to the International Classification of ROP (ICROP), was standardised in 1984, and updated in 1987 and again in 2005. ROP is characterised by using four components (Table 1): (i) location (zones 1 - 3); (ii) severity (stages 1 - 5); (iii) extent (circumferential location of the disease reported as clock hours); and (iv) plus disease (tortuosity of posterior retinal vessels).

Two important definitions are those of threshold ROP and prethreshold ROP (Table 2). Threshold ROP carries a risk of blindness of 50%, which can be reduced to 25% with treatment. Pre-threshold ROP can require either treatment or close observation – depending on the type. The various treatment options available for ROP include cryotherapy, laser ablative therapy, intravitreal antivascular endothelial growth factor (anti-VEGF) and retinal reattachment. Not all of these options are available in our setting.

In SA, approximately 1 in 5 of all VLBW babies is affected by ROP. A study at Chris Hani Baragwanath Academic Hospital found the incidence to be ~17%. In another study undertaken at Tygerberg Children’s Hospital in Cape Town, the incidence was found to be 21.8%. A study by Delport et al., at Kalafong Hospital, Pretoria, found the incidence of ROP to be 24.5%. The incidence at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) is unknown.

The present study aimed to review the screening programme for ROP in VLBW babies at CMJAH.

Methods
This study was undertaken at CMJAH, a tertiary care institution that serves as a referral centre for the primary care clinics and other hospitals in the area. It was a retrospective record review of all the VLBW babies admitted to CMJAH from 1 January 2013 to 31 December 2013, whether inborn or transferred in. Babies who died or were transferred out before day 28 of life were excluded from the present study.

Patient information was obtained from an existing neonatal VLBW database at CMJAH, which is kept for the purpose of clinical audit purposes. The database consists of standard information that is collected upon the discharge of each baby. Data are managed using REDCap (Research Electronic Data Capture) tools hosted by

### Table 1. The four components included in the classification of ROP[7]

<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
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<tbody>
<tr>
<td>Location</td>
<td>How far the developing retinal blood vessels have progressed</td>
</tr>
<tr>
<td>Zone 1: imaginary circle with optic nerve at the centre</td>
<td></td>
</tr>
<tr>
<td>Zone 2: extends from the edge of zone 1 to the ora serrata on the nasal side of the eye and half the distance to the ora serrata on the temporal side</td>
<td></td>
</tr>
<tr>
<td>Zone 3: the outer crescent-shaped area extending from zone 2 out to the ora serrata temporally</td>
<td></td>
</tr>
<tr>
<td>Severity</td>
<td>The stage of the disease</td>
</tr>
<tr>
<td>Stage 1: a demarcation line between normal and avascular retina</td>
<td></td>
</tr>
<tr>
<td>Stage 2: a ridge of fibrovascular tissue replaces the demarcation line</td>
<td></td>
</tr>
<tr>
<td>Stage 3: abnormal blood vessels and fibrous tissue develop on the edge of the ridge and extend into the vitreous</td>
<td></td>
</tr>
<tr>
<td>Stage 4: partial retinal detachment</td>
<td></td>
</tr>
<tr>
<td>Stage 5: complete retinal detachment</td>
<td></td>
</tr>
<tr>
<td>Extent</td>
<td>Circumferential location of the disease and reported as clock hours in the appropriate zone</td>
</tr>
<tr>
<td>Plus disease</td>
<td>Refers to the presence of vascular dilatation and tortuosity of the posterior retinal vessels in at least two quadrants</td>
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</tbody>
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### Table 2. Important definitions used in ROP screening[7]

| Threshold ROP | Zone 1 or 2: 8 cumulative clock hours of stage 3 with plus disease |
| Prethreshold ROP | Zone 1: Any ROP less than threshold |
| Zone 2: stage 2 ROP with plus disease |
| Stage 3 without plus disease |
| Stage 3 with plus disease but less than 8 cumulative clock hours |

### Table 3. ROP grading results in babies screened as inpatients

<table>
<thead>
<tr>
<th>Group</th>
<th>No ROP, n (%)</th>
<th>Grade 1 ROP, n (%)</th>
<th>Grade 2 ROP, n (%)</th>
<th>Grade 3 ROP, n (%)</th>
<th>Grade 4 ROP, n (%)</th>
<th>Grade not recorded, n (%)</th>
<th>Total, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early outcome group</td>
<td>28 (77.8)</td>
<td>2 (5.6)</td>
<td>2 (5.6)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>4 (11.1)</td>
<td>36</td>
</tr>
<tr>
<td>Late outcome group</td>
<td>81 (73.0)</td>
<td>11 (9.9)</td>
<td>5 (4.5)</td>
<td>2 (1.8)</td>
<td>1 (0.9)</td>
<td>11 (9.9)</td>
<td>111</td>
</tr>
</tbody>
</table>
the University of the Witwatersrand. All definitions in the database are according to the Vermont Oxford Network (VON) (www.vtoxford.org).

The ROP screening guidelines for CMJAH were derived from the SAMJ/2013 ROP screening guidelines, and state that all VLBW babies or those born at a GA <32 weeks should be screened at 4–6 weeks chronological age. In babies who were screened more than once, the worst grade of ROP recorded was used for the purpose of the study. Intravitreal anti-VEGF and surgery for ROP were available at CMJAH at the time of the study. Intravitreal anti-VEGF and surgery for ROP were available at CMJAH at the time of the study. Intravitreal anti-VEGF and surgery for ROP were available at CMJAH at the time of the study.

Prior to discharge, all VLBW babies at CMJAH were transferred to kangaroo mother care (KMC) once their current weight was >1 000 g, they were tolerating full enteral feeds and they were off supplemental oxygen. Whenever possible, these babies were transferred to regional hospitals for continuing care. The VLBW babies were discharged from hospital once they had reached a weight >1 600 g, were taking full oral feeds (either by cup or breast) and were maintaining their blood glucose levels. Babies were referred for ROP screening to the ophthalmologist at the discretion of the attending paediatric registrar, in accordance with the abovementioned guidelines. Babies in KMC were included in the screening programme. Results of the ROP screening were recorded on the daily charts and continuous variables by using measures of central tendency – mean and standard deviation – as the data were normally distributed.

Ethics approval
The study was approved by the Committee for Research on Human Subjects, University of the Witwatersrand, Johannesburg (clearance certificate No. M130947).

Results
A total of 572 (309 female) VLBW babies were admitted to the neonatal unit during the study period. A total of 162 babies were excluded. There were 128 deaths and 29 transfers to regional hospitals prior to 28 days of life. Five babies were transferred in to the unit after 28 days of life for surgical procedures; 2 died immediately and 3 were transferred back to their original hospitals within 2 days. The final sample therefore included 410 babies. The mean birth weight was 1 127 g with a standard deviation (SD) of 244.75 g, and the mean (SD) GA was 29 (2.74) weeks. The mean age at admission was 1 day (5.806) and the babies had a mean duration of stay of 28 (21.66) days. There were 147 babies in the early outcome group and 263 babies in the late outcome group (Fig. 1). ROP screening was documented in 147/410 (35.9%) VLBW babies. The ROP findings are summarised in Table 3. Plus disease was not found in any of the babies. Intravitreal anti-VEGF treatment was used in one baby and surgical treatment was documented in three babies.

Although the 147 babies in the early outcome group were not required to be screened as inpatients, ROP screening was carried out in 36 (24.5%) and of these 4 (11.1%) had evidence of ROP. Screening for ROP was undertaken in 111/263 (42.2%) babies in the late outcome group and 19 (17.1%) had evidence of ROP.

Discussion
This study shows that less than half of the VLBW babies at CMJAH eligible for inpatient ROP screening according to the hospital’s guidelines were actually screened for ROP.

More than one-third of babies were discharged before they had reached the required age for screening. Despite this, 24.5% of these babies were screened before 4 weeks of life. Of concern is that 11.1% of
these babies had ROP. This group of early discharges is important as they require outpatient ROP follow-up. It is not known whether these babies attended screening for ROP as outpatients, so it is possible that a number of babies with ROP were missed. Education of caregivers in this group is essential, as defaults to follow-up are at risk of presenting with more severe grades of ROP and increased morbidity.

Although a true prevalence for ROP at CMJAH for 2013 cannot be calculated, as a result of the low level of screening, ROP was found in 15.6% of VLBW babies, which is similar to the 17% rate reported at Chris Hani Baragwanath Academic Hospital.[10] Other SA studies reported slightly higher rates – 21.8% at Tygerberg Children’s Hospital[13] and 24.5% at Kalafong Hospital.[14]

This review shows that the inpatient ROP screening at CMJAH is not optimal and needs to be improved. Inpatient ROP screening was not carried out in 57.8%. Babies at risk need to be promptly identified. The attending medical staff (interns, medical officers, registrars and consultants) should to be familiar with the guidelines. Junior staff will need to be educated on the harms of oxygen therapy and the subsequent complication of ROP and its consequences. Although it may seem attractive to delay the discharge of VLBW babies until they have achieved the recommended age for ROP screening, this is not feasible because of high patient numbers and extreme pressure for beds.

Adjusting the screening protocol to allow ROP screening at a younger age in those babies who will be discharged before 28 days of age would be a simpler solution and would prevent missed opportunities to identify babies with ROP.

No babies were recorded to have plus disease. These data may have not been captured on discharge, were truly not present or may have been under-reported by the ophthalmologist performing the screening. Bigger babies are also at risk of ROP. The 2013 SAMJ ROP guideline suggests that premature babies with weights between 1 500 g and 2 000 g may also be at risk if they have risk factors; if oxygen monitoring in this group of babies has been suboptimal then screening should be considered.[11] This group of babies was not included in the present study, but should not be overlooked in screening programmes for ROP.

Ideally, an electronic prospective data capture system needs to be implemented to capture all the results of ROP screening – both inpatient and outpatient. This would only be possible in conjunction with the Department of Ophthalmology, especially regarding the outpatient screening. This will assist greatly with future research and in gauging the incidence of ROP at CMJAH.

**Study limitations**

One limitation is the design of the study – the retrospective nature of the study means a precollected dataset was used. ROP information is not available for babies on the low-birth-weight (LBW) database who may have a GA of <32 weeks but a weight of >1 500 g. Another potential limitation is that of inter-observer error in classifying the grade of ROP present, as different ophthalmology registrars did the screening, with different levels of skill and experience.

**Conclusion**

More than half of VLBW babies who met criteria for ROP screening according to CMJAH ROP screening guidelines were not screened during their inpatient stay. Efforts need to be intensified to identify these babies and screen them prior to discharge.

Records for outpatient ROP screening were not well organised and not easily accessible at both the neonatal follow-up clinic and the ophthalmology unit. There is a need for a co-ordinated database between the two specialties. In this regard, a true prevalence for ROP at CMJAH cannot be established.

Screening for ROP should include all babies with a GA of <32 weeks (even if their weight is >1 500 g). In addition, babies weighing between 1 500 g and 2 000 g with risk factors for ROP should not be omitted from screening programmes.

**References**