

Outcomes of surgery for stage 4 and 5 retinopathy of prematurity in a developing country

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ABSTRACT

Objective: To assess anatomical and visual outcomes plus complications of surgeries in patients with stage 4 and 5 retinopathy of prematurity in a tertiary eye care centre in Bangladesh.

Methods: Retrospective case series of all patients that underwent surgery for stage 4 and 5 retinopathy of prematurity between January 2015 and January 2018 was carried out. Anatomic outcomes, qualitative visual acuity as well as the complications were assessed.

Results: Thirty three eyes of 25 patients were recruited in the study (12 male and 13 female). Overall 22 (66.7%) of the eyes had complete retinal re-attachment. The percentage for complete re-attachment for stage 4A, 4B, and 5 were 89.5%, 66.7% and 12.5% respectively. Overall 19 eyes (57.6%) had ability to fix and follow objects. This included 14 eyes (73.7%) in stage 4A, 4 eyes (66.7%) in stage 4B and 2 eyes (25.0%) in stage 5. The commonest complications noted were cataracts (15.2%), vitreous haemorrhage (15.2%) and glaucoma (9.1%).

Conclusion: Anatomical outcomes of surgery for stage 4A retinopathy of prematurity are very encouraging while those of stage 4B and 5 are poorer. Consequently, visual outcomes for stage 4A are also better than those for stage 4B and 5.

Key words: Retinopathy of Prematurity, Outcomes, Surgery, Bangladesh

INTRODUCTION

Retinopathy of Prematurity (ROP) is a disease resulting from abnormal retinal vascular development. The main predisposing risk factors are prematurity and low birth weight^{1,2}. Paediatric care around the world is improving. As a result increasingly more premature infants are surviving and that has raised the incidence of ROP to be one of the leading causes of child-hood blindness³. Dedicated ROP screening programs are now part of many neonatal care services and prompt treatment with laser when indicated has become the practice. Recently attention has also focused on use of anti-vascular endothelial growth factors for stage 3 ROP. The bevacizumab eliminates the angiogenic threat of retinopathy of prematurity (BEAT-ROP) study showed significant benefit of intravitreal bevacizumab for stage 3 zone 1 ROP⁴ which hitherto was only managed by ablation.

Even though it has been shown that ablation therapy improves the outcomes of children with severe ROP³, some children still progress to latter stages of the disease and develop retinal detachment^{1,3,5,6}.

Advanced stages of ROP (stage 4 and 5) usually require surgical intervention⁷ to preserve both the anatomical and functional integrity of the eye. Some of the surgical methods employed in this regard include Scleral Buckling (SB), Lens-Sparing pars-plana Vitrectomy (LSV), pars-plana Lensectomy with Vitrectomy (LV) and open sky

vitrectomy^{1,7}. The choice of method depends on the stage of ROP and characteristics specific to each eye^{7,8} such as the extent of the fibrovascular membranes and its relation to the lens as well as surgeon's preferences.

Even though surgical outcomes for the various stages vary widely, in stage 4A the macula is preserved and thus timely reattachment of the peripheral detached retina can halt the progression of the disease and preserve central vision. Consequently children with stage 4A ROP tend to have better outcomes⁹. Once the detachment encroaches on the macula however, outcomes tend to be more guarded and can often lead to irreversible loss of vision^{1,8}. In this study we present the results of surgery for stage 4 and 5 ROP in a tertiary institution in a developing country. We describe visual outcomes, anatomical results and complications associated with these surgeries in our setting. The results will inform us on the capabilities of our ROP program in terms of managing latter stages of the disease as well as give an idea of capabilities of similar programs especially in other developing countries.

MATERIALS AND METHODS

We carried out a retrospective consecutive case series of all patients with stage 4 or 5 ROP who underwent surgery. The study was carried out at Ispahani Islamia Eye Institute and Hospital which is a tertiary ophthalmic care centre in Bangladesh between January 2015 and January

2018. It was authorized by the institution's review board and performed in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from the parents or guardians of all participants before examination under anaesthesia and surgery. Case files were identified and retrieved from the institutions medical records department and the following demographic data recorded: date of birth, sex, gestational age and birth weight.

The following clinical data was obtained: whether the infant had undergone laser photocoagulation and or anti-vascular endothelial growth factor treatment before surgery, stage of ROP, presence of plus disease, type of surgery done, intra-operative complications, post operative complications, duration of follow up after surgery, anatomic status of the retina on last follow up and the visual acuity at the last follow up. The stages of ROP were defined in accordance with the international classification of ROP and plus disease¹⁰.

Data was analyzed using SPSS version 20.0. A p-value of <0.05 was considered statistically significant. The primary outcomes were anatomical attachment and presence or absence of fixation ability. Anatomic outcome was categorized as either fully attached retina (both within and without the arcades), attached only at the posterior pole (within the arcades) or not attached at all (posterior pole off).

The surgical techniques: All the surgeries were done by two vitreoretinal surgeons (NN and SKD) who have also undergone training in ROP. The surgical procedures in this series included SB, LSV and LV and have been described elsewhere^{7,11,12}. In our case we employed the 3 port technique for vitrectomy and used vitreous cutter and membrane peeler cutter scissor. We used 23 gauge systems. The eye was entered 1mm from the limbus via the pars plicata. Core vitrectomy was performed and all membranes peeled off as much as possible. Lensectomy was carried out for those eyes needing more extensive anterior dissection close to the lens. There after fluid-air exchange was performed. The sclerotomies were closed, and the child positioned face down.

SB involved placement of an encircling band under the rectus muscles and as close to the ridge as possible. We used mattress sutures in each quadrant to further secure the band. When the surgeon was satisfied with the amount of indentation achieved, paracentesis was then carried out to normalize intraocular pressure. We routinely remove the band at 6 months post operatively.

Postoperatively, all patients were examined in the clinic or under anaesthesia. The interval of examination depended on the surgeon's judgment, informed by individual patient and ocular characteristics. Visual rehabilitation was done in conjunction with the paediatric ophthalmologist and the low vision specialist as deemed appropriate. Aphakic correction was provided by either contact lenses or spectacles.

RESULTS

A total of 33 eyes of 25 children were enrolled in this review (12 male and 13 female). The mean gestation age was 31 ± 2.8 weeks and the mean birth weight was 1414.4 ± 292.1 grams. The median duration of follow up after surgery was 5.9 months (range 1 month 4 days to 16 months 2 days). Table 1 shows the patient demographics and characteristics of the operated eyes.

Table 1: Demographic data of the patients and status of operated eye

Characteristics	
No of patients (eyes)	25(33)
Sex (n), Male/Female	12/13
Gestation age (Weeks), mean $\pm$ SD	31.0 $\pm$ 2.8
Birth weight (grams) mean $\pm$ SD	1414.4 $\pm$ 292.1
Prior treatment, Laser/laser+Avastin/None	24/7/2
Surgery type, LSV/ LV/ SB	19/6/8
ROP stage at time of surgery, 4A/4B/5	21/1/11
Plus disease, Present/ Absent	6/27

Abbreviations: LSV=Lens sparing vitrectomy, LV=Lensectomy with vitrectomy, SB=Scleral Buckling

Anatomic outcomes: Overall out of the 33 eyes that underwent surgery, 22 (66.7%) had fully attached retina, 5 (15.2%) had attachment only at the posterior pole while 6 (18.2%) remained unattached. Of the 19 eyes with stage 4A disease, 17 (89.5%) had fully attached retinas while 2 (10.5%) had attachment only at the posterior pole. In stage 4B, 4 out of 6 eyes (66.7%) had fully attached retina, one was attached only at the posterior pole while one remained unattached. In stage 5, 6 out of 8 eyes (62.5%) remained unattached, 2 (25.0%) were attached only at the posterior pole while one eye (12.5%) had fully attached retina. All except one eye in stage 4A (94.7%) had undergone preoperative laser ablation as well as 4 out of 6 eyes in stage 4B (66.7%).

Visual outcomes: Visual outcomes varied across the groups. Overall 19 out of the 33 (57.6%) eyes were able to fix and follow objects, while 6 (18.2%) eyes had light perception. The remaining 8 (24.2%) eyes could not be assessed either because the child had neurologic conditions (3 eyes) or because the child was uncooperative (5 eyes). In stage 4A, 14 (73.7%) eyes could fix and follow objects while 5 (26.3%) eyes could not be examined. In stage 4B there were 4 (66.7%) eyes that could fix and follow objects, 1 (16.7%) eye had light perception while another 1 (16.7%) eye could not be examined. In stage 5, 2 (25.0%) eyes were able to fix and follow objects while 3 (37.5%) eyes had light perception and another 3 (37.5%) eyes could not be examined.

Complications: There were no recorded intra-operative complications. However, post operatively, 5 (15.2%) eyes

developed cataracts and had to undergo cataract surgery. Three (9.1%) eyes developed glaucoma and underwent glaucoma surgery (trabeculectomy plus trabeculotomy). Intraocular pressure was controlled thereafter. Five (15.2%) eyes developed vitreous haemorrhage of which 4 had plus disease pre-operatively. All of these were managed conservatively. The other complications observed included uveitis (2 patients), transient hypotony (1 patient) and strabismus (1 patient).

DISCUSSION

Early and timely interventions in ROP is key in forestalling the progression of the disease to retinal detachment. For children who develop detachment, surgery presents a viable option for management. The main aim of the various surgical modalities employed is to relieve traction on the retina and hence reattach it to the retinal pigment epithelium. Scleral buckling achieves this by indenting the globe thus counteracting the forces exerting traction on the retina¹³. It is often used alone or in combination with vitrectomy especially in eyes with extensive traction anterior to the equator⁷. Vitrectomy on the other hand not only physically eliminates the tractional membranes but is also hypothesized to remove growth factors that contribute to vascular activity¹. Lensectomy is often added to enable the surgeon to access more anteriorly located membranes than would otherwise not be reachable without the risk of touching the lens. It can also be done to advance clarity of fundus view and to rid the lens in case of inadvertent lens touch with cataract development.

In stage 4A ROP, outcomes without interventions have been reported to be poorer than when surgery is rendered¹. In our study we found a complete attachment rate of 89.5% (17/19) eyes in stage 4A. In addition, 14 (73.7%) eyes were able to fix and follow objects. Similar findings have been reported by Capone and Trese¹² who studied outcomes in patients who had undergone LSV. They found that 90.0% (36/40) of eyes showed retinal reattachment and fixation behavior at their last follow-up visit. Elsewhere, Hubbard *et al*¹⁴ found that 21/25 (84.0%) of eyes with stage 4A ROP had complete retinal reattachment after surgery and 19/25 (76.0%) were able to fix and follow. These findings thus demonstrate that for stage 4A eyes prompt intervention can yield good outcomes.

Outcomes for detachments involving the macula in stage 4B ROP are worse compared with stage 4A¹. In this study 4 (66.7%) eyes had fully attached retina and all 4 (66.7%) had fixation and following ability. These numbers are however too small to establish a strong trend and the qualitative nature of the measured visual acuity make direct comparisons with other studies difficult. However a review of case series by Asano *et al*¹ revealed that only 12.0% of the 141 eyes had measurable acuity better than 20/2000. In addition, El Reyes *et al*¹⁵ found full attachment in 73.2% (41/56) eyes, and in terms of

visual acuity they found that 57.2% (32/56) eyes had vision worse than 20/800. It's apparent therefore that once the macula is involved outcomes tend to be more guarded. Surgeons should thus be vigilant and intervene earlier when detachments are still outside the macula.

Anatomical and visual outcomes for stage 5 surgeries are even worse compared to stage 4B. In this study out of the 8 eyes in stage 5 only 1 (12.5%) eye had full retinal attachment, 2 (25.0%) had attachment only at the posterior pole while the rest (62.5%) remained unattached. In addition, only 2 (25.0%) eyes were able to fix and follow objects. Similarly, Choi *et al*¹⁶ reported full retinal attachment in only 13% of cases and partial attachment in 27.6%, whereas fixation and following ability was noted in only 17.2% of the eyes. Stage 5 eyes tend to have very extensive fibro-proliferative membranes making surgery not only difficult but the settling of the retina is also less predictable.

In this study most patients with stage 4A and 4B disease had undergone preoperative laser ablation. However because of the low numbers involved, the advantage conferred by laser in this study could not be analyzed. However, elsewhere El Reyes *et al*¹⁵ observed that retinal ablation was associated with better anatomical outcomes. Laser ablates the ischemic retina thus reducing oxygen demand by the retina. As a result there's down regulation of vascular endothelial growth factor and subsequent involution of abnormal new vessels hence slowing fibro-proliferation and traction on the retina. It's thus desirable that whenever possible ablation therapy should be done before surgery. However this is not always possible as not all children are captured by the screening programs and so some show up when the retina is already extensively detached.

In our study the foremost complications were cataract in 5 (15.2%) eyes, vitreous haemorrhage in 5 (15.2%) eyes and glaucoma in 3 (9.1%) eyes. Similar complications have been reported by Choi *et al*¹⁶.

Notably, of the 5 eyes in our study that developed vitreous haemorrhage post operatively, 4 (80.0%) eyes had plus disease. Hartnet¹⁷ suggested that the presence of plus disease at the time of LSV could be a cause of surgical failure. In addition, Xu *et al*¹⁸ reported better anatomic and visual outcomes in eyes with vascularly active disease that had undergone preoperative anti-VEGF injection compared to those that had not. They also reported no vitreous haemorrhage among those eyes that received anti-VEGF compared to 2 (20%) among those that did not. In spite of the benefits of anti-VEGF, the surgeon sometimes has no choice but to operate eyes with plus disease or risk further progression while waiting for regression.

A limitation of the current series is that it is a retrospective study. Secondly the visual acuity records were qualitative and thus limited the comparison we could draw to fully understand the impact of the operations. Thirdly, sample sizes in the sub groups were small

making generalizations difficult to draw. We also had a limited follow up as some patients were lost to follow up. That meant that long-term complications such as re-detachments could not be ascertained.

CONCLUSION

Our study shows that surgical and visual outcomes for stage 4A ROP are good while the outcomes for stage 4B and 5 are poorer. Surgeons should therefore endeavor to operate on the eyes with retinal detachment due to ROP early before the macula gets involved.

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