Evaluation of a revised care plan for babies with retinopathy of prematurity during SARS-CoV-2 pandemic in India

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Purpose: To analyze the impact of a revised care plan for retinopathy of prematurity (ROP) during SARS-CoV-2 pandemic in a tertiary eye care facility in eastern India. Methods: In a retrospective study, we analyzed the medical records of babies managed for ROP during the peak of the SARS-CoV-2 pandemic, with particular reference to the challenges, and the revised strategies addressing travel restrictions for five months, from April to August 2020. The strategy included selective referral (babies with higher treatment probability), longer follow-up intervals (babies with non-alarming findings), use of locally available workforce, and teleconsultation whenever feasible. Results: In the given period, 222 babies were examined versus 624 in the preceding year (P = 0.001). The average gestational age, birth weight, and postmenstrual age at presentation were 30.4 weeks, 1.31 kg, and 37.7 weeks, respectively. The first examination was on time in 40.1% of babies but was delayed by a median of 23 days in the remaining babies. In the cohort, 56.7% of babies had any ROP, and 27.9% required treatment (versus 8.8% in the previous year; P < 0.001). The intravitreal anti-vascular growth factor (anti-VEGF) injection was more often used than in the previous year (n = 72 vs 36; P < 0.0001). The treatment outcome was comparable before and after the SARS-CoV-2 lockdown period. There was no report of health issues among the care providers attributable to ROP care. Conclusion: The revised strategy resulted in a smaller pool of babies screened but a larger proportion of babies treated for ROP. This strategy could be used more profitably in future ROP care.

Key words: COVID-19, lockdown, retinopathy of prematurity, SARS-CoV-2 pandemic

In 2019, the virus SARS-CoV-2 emerged as a pandemic that resulted in drastic lifestyle changes, including disruption in health care delivery.[1–3] Being a highly contagious airborne and aerosol mediated infectious disease, strict social distancing, and restrictions on travel and social gatherings were imposed as some of the essential and effective ways in containing the infection and preventing community spread. While there were restrictions on the functioning of all elective services, essential services had to continue with appropriate preventive measures.

Retinopathy of prematurity (ROP) is an essential ophthalmic and health care condition. It affects immature retinal vasculature due to low birth weight and/or prematurity. Being a potential vision-threatening and time-bound disease, it requires urgent attention and has been categorized as an essential service by national and international ophthalmic societies.[4–7] However, there is always concern for an increased risk of transmission of SARS-CoV-2 infection between babies and care providers during treatment.[8] The infants and toddlers could be asymptomatic carriers, so implementing source control measures such as wearing a face mask and maintaining social distancing in this age group is difficult. Frequent and sustained cry of babies is quite common, increasing the risk of aerosol generation and transmission. In such a situation, one needs a balance between care given to the babies and safety of the care providers. The present study examined these factors to weigh their impact on ROP care.

Methods

This retrospective observational study was conducted at a tertiary eye care institute in eastern India. For longer than a decade, the institute has provided in-person ROP screening at the institute eye care institute has provided in-person ROP screening at the institute for babies treated for ROP. This strategy could be used more profitably in future ROP care.
Table 1: ROP Care: Protocol in Brief

| Before Examination |
|---------------------|
| Screening of babies and parents for COVID-related signs and symptoms |
| Protective wear for parents and the care provider (N95 mask, face shield, gloves, sanitizer), social distancing |
| ROP care staff confirming the need for ROP screening based on the eligibility criteria |
| Parents bring the baby near the ROP screening room; application of dilating drops with no touch technique and quick history at a distance |
| Alcohol-based hand sanitizers available at all important areas |

| In Examination Room |
|---------------------|
| Waiting area and examination rooms are provided with adequate ventilation and periodic meticulous disinfection |
| Parent keeps the baby on sterile steel table and leaves the examination room |
| Nesting of infants, assisting nurse with mask, visor and gloves |
| Ophthalmologist with mask visor and gloves quickly examines the eyes and goes back to his seat; baby is handed over to the parents and the indirect ophthalmoscope and 20 D lenses are cleaned |
| Fundus imaging was restricted to severe cases or treatment warranting ROP |

| Examination findings are entered in our EMR system |
| Counselling of parents over phone or at a distance |
| Areas with a possibility of contamination (desk, table, chairs) were sterilized between patients sterilized with Sodium Hypochlorite |

| Intervention |
|--------------|
| Laser photoagulation done at the institute or in a NICU setup |
| Anesthetists or neonatologist available as standby with protective wear |
| Cases positive for COVID antigen are treated with full PPE kit |
| Intravitreal avastin given in the operating rooms; bilateral injections on the same day preferred to minimize hospital visits |
| For confirmed COVID positive patients with retinopathy warranting urgent treatment, service is provided using full PPE kit by the care provider |

| Counselling |
|-------------|
| Counselling of parents was done telephonically or at a distance, whichever feasible |
| Follow-up |
| Infants with higher BW, older GA, good weight gain, lower collateral health issues, no or lesser duration of oxygen supplementation, nonalarming fundus finding in the initial visits, immature retina in zone III were followed up at longer interval |

COVID: Coronavirus disease, EMR: Electronic medical record, NICU: Newborn intensive care unit, PPE: Personal protective equipment, ROP: Retinopathy of prematurity

and bedside for babies admitted in different newborn care units in two cities (Bhubaneswar and Cuttack) of Odisha, India. Additionally, the institute also assists the local ophthalmologists trained in ROP (with different levels of competence) in the peripheral districts of the state. Suspected and treatment warranting ROP babies are referred for confirmation or additional care. The study compared the outcome of ROP care for five months, from April to August 2020, at the height of the COVID-19 lockdown and a similar period in the previous year, from April to August 2019. The strategy adopted to provide ROP care while ensuring safety was analyzed [Table 1]. The most important ones were the safety measures against SARS-CoV-2 transmission and a revised ROP care plan to minimize travel and hospital visits. The latter included a longer follow-up interval of babies likely to have less severe ROP evident from the perinatal profile (e.g., good weight gain, higher GA, higher BW, shorter stay in NICU, lower co-morbidities like sepsis, apnea, respiratory distress, no or shorter duration of oxygen supplementation, etc.), eyes with no ROP, immature retina or non-alarming retinal findings during the examination. Major safety measures included screening protocols for the babies and care providers against SARS-CoV-2-related signs and symptoms, ensuring social distancing and personal protective equipment (PPE) against disease transmission at every stage of care. Additionally, the strategy also included teleconsultation, periodic dialogue, phone call reminders to the parents about the local follow-up post-intervention, online meetings with the local ophthalmologists and pediatrician on the need and timing of examination of the babies based on perinatal history. A common practice adopted during this period included history-taking over the phone and providing counselling about procedures before the arrival of the baby and pupillary dilation with monitoring immediately at check-in. This reduced the chair time and face-to-face conversation in the hospital.

This was a part of an ongoing study on the demographics, clinical profile, and outcome of babies evaluated for ROP in the eye institute since 2014 and has been approved by the institutional Review Board (2014-29-IM-6). The study followed the tenets of the Declaration of Helsinki. The management followed the institutional protocol, including the consent from the parents of the babies for sharing the de-identified data for education and research. Babies with inadequate or incomplete details were excluded from the analysis. The collected data included the demographic profile, gestational age (GA), birth weight (BW), post-menstrual age (PMA) at examination, ROP status, treatment modality, and outcome; additionally, we also collected history of any SARS-CoV-2-related infections both before and by a telephone call post treatment, up to a week after the hospital visit. All the classifications were performed as per the Cryotherapy for Retinopathy of Prematurity (CRYOROP), International Classification of Retinopathy of Prematurity (ICROP)-revised,[10] and Early Treatment for Retinopathy of Prematurity (ETROP) studies.[11] The term “hybrid ROP” was used to describe ROP with ridge tissue, similar to staged ROP and flat new vessels, simulating aggressive posterior retinopathy of prematurity (APROP), in the same eye, described by Sanghi et al.[12] The ROP management protocol was revised at the peak of SARS-CoV-2 in India,[14–16] and the previous year data were gathered from the ophthalmologists who managed these babies.[14–16]

Data were entered in a Microsoft Excel spreadsheet, and the final analysis was done using Statistical Package for Social Sciences (SPSS) software (IBM, Chicago, USA, version 21.0). The presentation of the categorical variables was done in absolute numbers and percentages. In addition to calculations like mean, median, mode, and range, the Chi-squared, Mann–Whitney U, and Fisher’s exact tests were used to assess the statistical significance. A P value of <0.05 was considered statistically significant.
Results

The number and profile of the babies with ROP during the study vis-a-vis the control (similar) period in the previous year [Tables 2 and 3] showed many differences, as noted below.

Tables 2 and 3 and Fig. 1 show the impact of SARS-CoV-2 and differences. There was a large dip in the babies cared for ROP during the study compared to a similar period of five months in the previous five years. In contrast, the number of babies treated were more or less identical to the previous year [Fig. 2]. The screening numbers of babies had increased between 2015 and 2019 because of greater awareness; despite it, there was a decline in the number of screened babies in 2020. It was nearly three times less, 222 against 624, for a similar period in 2020 and 2019, respectively, and was significant (P = 0.001). The decrease (n = 244) was higher for bedside screening (outside the institute) than those referred and examined at the institute (n = 158) and was significant (P = 0.0001) [Table 2]. But the proportion of babies identified with ROP during the study period was significantly higher than the previous year (56.7% vs 34.3%; P < 0.0001). The proportion of babies requiring treatment among those screened for ROP was 2.78 times higher during the study period than in the corresponding period in 2019 (24.47% vs 8.8%, P < 0.0001).

Additionally, in 2019, the proportion of babies with APROP was higher, and the number of babies with threshold ROP was higher during the study period [Table 3]. The proportion of babies with advanced ROP (stages 4 and 5) was slightly higher during the SARS-CoV-2 period (6 of 126 with ROP; 4.76% vs 7 of 214 with ROP; 3.27%). The difference was statistically significant for stage 5 ROP (P = 0.044) but not for stage 4 ROP (P = 0.086). There was a delay in the first screening in 59.9% of babies during the SARS-CoV-2 time compared to 34.93% in the previous year, and this was statistically significant (P < 0.0001). We followed the recommended standard operating procedures of ROP care revised for the pandemic by the Indian ROP society[3] and the institutional hospital infection control committee [Table 1].

The eyes lost to follow-up during the study period for various reasons were two times higher (20 vs 10) than the year-earlier period, but the difference was not statistically significant (P = 0.109). The proportion of babies treated with

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**Table 2: Characteristics of babies cared for ROP during the study period and in the year before**

|                  | Study period 2020 | Same period 2019 | P    |
|------------------|-------------------|------------------|------|
| Total numbers of babies screened | 222 (444 eyes) | 624 (1248 eyes) | 0.001* |
| Fresh            | 181              | 544              |      |
| Follow-up        | 41               | 61               |      |
| At the Institute | 141 (63.51%)     | 299 (47.16%)     | 0.0001* |
| Bedside screening at NICU | 81 (36.8%)   | 325 (52.08%)     |      |
| GA (wks)         | 31 (30-33)       | 32 (30-34)       | 0.0004* |
| BW               | 1334 (1100-1675) | 1450 (1160-1725) | 0.059 |
| Babies with delayed 1st screening | 133 (59.90%) | 218 (34.93%) | <0.0001* |

*Chi-squared test, †Mann-Whitney U test. BW: Birth weight; GA: Gestational age

**Table 3: Profile of retinopathy in babies cared for ROP during the study period versus that in the previous year**

|                  | Study period 2020 | Same period 2019 | P    |
|------------------|-------------------|------------------|------|
| Babies screened detected with ROP | 126 (56.75%, n=222) | 214 (34.29%, n=624) | <0.0001* |
| Babies with treatment warranting ROP | 62 (27.92%, n=222) | 55 (8.8%) | <0.0001* |
| APROP            | 27 (21.77%)       | 44 (43.13%)      | 0.343* |
| Threshold        | 41 (33.06%)       | 14 (13.72%)      | <0.0001* |
| Hybrid ROP       | 16 (12.90%)       | 19 (18.62%)      | 0.108* |
| HRPTH ROP        | 34 (27.41%)       | 18 (17.64%)      | 0.002* |
| Stage 4          | 4 (03.22%)        | 05 (4.90%)       | 0.086* |
| Stage 5          | 2 (1.61%)         | 02 (1.96%)       | 0.044‡ |
| Treatment advised but not done | 08 (12.90%) | 7 (12.72%) | 0.113* |

*Chi-squared test, ‡Fisher’s exact test. APROP: Aggressive posterior retinopathy of prematurity, HRPTH: High-risk pre-threshold

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Figure 1: Babies with ROP cared for during the study period (1 April to 31 August 2020) compared to the same period in years prior

Figure 2: Babies treated for ROP during the study period (1 April to 31 August 2020) compared to the same period in years prior
intravitreal anti–vascular growth factor (anti-VEGF) injections was higher during the study period [Table 4], and the difference was statistically significant (P < 0.0001). The treatment outcome was nearly comparable between the study period and the previous years (P = 0.175). We did not come across any incidence of transmission of SARS-CoV-2 between those cared for and the caregiver related to ROP care.

Table 4: Eyes treated with various modalities of treatment during the study period versus previous year and outcome

| Treatment Modality | Study period 2020 109 eyes (Babies: 62) | Same period 2019 96 eyes (Babies: 55) | P     |
|-------------------|----------------------------------------|-------------------------------------|-------|
| Laser             | 33 eyes                                | 34 eyes                             | 0.461*|
| Intravitreal anti-VEGF | 72 eyes                                | 36 eyes                             | <0.0001*|
| Injection+laser   | 12 eyes                                | 23 eyes                             | 0.014*|
| Laser+surgery     | 01 eye                                 | 00 eye                              | 1    |
| Surgery           | 02 eyes                                | 04 eyes                             | 0.422*|
| Inj + Laser + Surgery | 0 eye                                 | 02 eyes                             | 0.218*|

*Chi-squared test, †Fisher’s exact test. Anti-VEGF: Anti-vascular endothelial growth factor

Discussion

The World Health Organization declared the SARS-CoV-2 respiratory infection, with high morbidity and mortality, a public health emergency on 30 January 2020 and later as a pandemic on 11 March 2020. As the mode of transmission was primarily as aerosols, control measures such as lockdowns, and travel restrictions of varying severity were put in place by the governments across the globe. This led to disruption in the delivery of health care globally. It also affected the timely screening of at-risk babies for ROP, an essential component of ROP care. It resulted in a significant decrease in the number of babies needing ROP care than in the years prior [Fig. 1]. Others have also made similar observations.[13–15] Many factors were responsible for this behavioral change and these included restricted transport facilities, fear of disease transmission among the parents, hesitancy of ophthalmologists, unavailability of the required number of personal protective equipment (PPE) kits for ophthalmologists (in India and other similar economy countries), and often re-deployment of ophthalmologists for SARS-CoV-2 duties in India.

In this unprecedented and new scenario, it became necessary for the referring pediatricians and the care providers to judiciously modify the screening criteria to reduce the burden of the health care providers without grossly neglecting the babies at risk. It required multi-disciplinary coordinated work. The screening guidelines were redesigned in consultation with the in-house hospital infection control strategy group, the Indian ROP society, the Vitreoretinal society of India (VRSI), and the All India Ophthalmological Society (AIOS).[14–16] The decrease in the number of babies screened was higher for bedside...
screening. Since this type of screening is actually initiated by the hospital and ophthalmologists, it should not have been affected by the pandemic. However, due to the ongoing pandemic, we intentionally restricted the frequency of travel by our staff to far-off peripheral districts, taking advantage of our locally available ROP workforce and teleconsulting services.

We already had a ROP network spread to some peripheral districts of Odisha, sustained by the local ophthalmologists trained in the past.[9] We had a formal discussion, training, and interaction, virtually, during this period devising the best use of the existing ROP skills in ensuring less referral without missing a treatment-warranting baby. They also helped in the follow-up care of babies after treatment (injection, laser) and babies identified with immature retina and low-risk, pre-threshold ROPs. Some of the high-volume peripheral newborn care units had pediatric retinal imaging device facilities, enabling a teleconsultation with the local ophthalmologist; it reduced travel for ROP care. The emergency approval of the long-pending policy for teleconsultations as legally valid by Government of India also helped to modify our strategy. Despite a decreased pool of babies referred for ROP care, the changed strategy helped us treat the required number of babies in the study period. But due to the reduced number of screened babies, the percentage of babies requiring treatment during the study period was at least two times higher than in the year 2019 (27.92% vs 8.8%) and about 5.5 times higher than in the last few years reported for the previous years (27.92% vs 5.06%).[10] This is in contrast to the earlier reports from India that documented a reduction in the number of babies screened and/or treated [Table 5].[13] This could be the result of several factors and include delayed presentations, a tighter screening aimed at detecting babies with ROP or treatment requiring ROP, reducing the number of follow-up of babies with fundus changes of less concern (such as immature retina with no ROP), teleconsultation of ROP images in some, and telephonic consultation of referring ophthalmologists.[10] In this reported period, more babies were treated with intravitreal anti-VEGF injections than laser, even for babies suitable for both modalities compared to other reports [Table 5]. The reasons could be the increased preference by the treating doctors for a shorter procedure and availability of a network of ROP care in some peripheral districts with scope for post-injection follow-up care.

There were two limitations to this study: One, it was a retrospective study, with all its inherent limitations; two, despite our efforts, we could not find out the number of babies who could not be timely screened and treated. But the greatest learning was our ability to rapidly build robust teams and re-strategize our health care protocols to meet unprecedented emerging challenges.

**Conclusion**

The SARS-CoV-2 pandemic is still looming large (at the time of the manuscript writing). Nevertheless, we should benefit from this experience and suitably modify our approach to avoid missing any babies with treatable ROP. Our strategy must also aim to reduce the number of hospital visits and prioritize the babies who need treatment. The new strategy and timely modification would be useful in similar situations.

**References**

1. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of corona virus disease 2019 in China. N Engl J Med 2020;382:1708-20.
2. CDC COVID-19 Response Team. Severe outcomes among patients with corona virus disease 2019 (COVID-19)-United States, February 12-March 16, 2020. MMWR Morb Mortal Wkly Rep 2020;69:343-6.
3. World Health Organisation (WHO). WHO Director-General’s opening remarks at the media briefing on COVID-19 11 March 2020. Available from: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19-11-march-2020. [Last accessed on 2020 Jul 30].
4. Sengupta S, Honavarg S, Sachedev MS, Sharma N, Kumar A, Ram J, et al. All India Ophthalmological Society-Indian Journal of Ophthalmology consensus statement on preferred practices during the COVID-19 pandemic. Indian J Ophthalmol 2020;68:711-24.
5. Gupta V, Rajendran A, Narayanan R, Chawla S, Kumar A, Palanivelu MS, et al. Evolving consensus on managing vitreoretina and uvea practice in post-COVID-19 pandemic era. Indian J Ophthalmol 2020;68:962-73.
6. Vinekar A, Azad RV, Dogra MR, Jalali S, Bhende P, Narendran V, et al. For the Indian Retinopathy of Prematurity Society. Retinopathy of prematurity screening and treatment guidelines during the COVID19 lockdown 2020. Available from: https://sites.google.com/view/iropsociety/newsroom?authuser=0. [Last accessed on 2020 May 05]. 13. Project operational guidelines.
7. American Academy of Ophthalmology. 2020, March 27. List of urgent and emergent ophthalmic procedures. Available from: https://www.aao.org/headline/list-of-urgent-emergent-ophthalmic-procedures. [Last accessed on 2020 Jun 09].
8. Samsons JS, Graf EH, Townsend S, Hoegg CL, Smathers PA, Coffin SE, et al. Outbreak of adenovirus in a neonatal intensive care units: Critical importance of equipment cleaning during inpatient ophthalmologic examinations. Ophthalmology 2019;126:137-43.
9. Padhi TR, Pradhan L, Padhy SK, Meherda A, Samantaray B, Patro KK, et al. Retinopathy of prematurity care in peripheral districts in Odisha, India: Pilot for a sustainable model. Indian J Ophthalmol 2020;68(Suppl 1):S124-7.
10. International Committee for the Classification of Retinopathy of Prematurity. The International classification of retinopathy of prematurity revisited. Arch Ophthalmol 2005;123:991-9.
11. Early Treatment for Retinopathy of Prematurity Cooperative Group. Revised indications for the treatment of retinopathy of prematurity: Results of the early treatment for retinopathy of prematurity randomized trial. Arch Ophthalmol 2003;121:1684-94.
12. Singh G, Dogra MR, Dogra M, Katodh D, Gupta A. A hybrid form of retinopathy of prematurity. Br J Ophthalmol 2012;96:519-22.
13. Katodh D, Singh SR, Kumar P. Impact of the COVID-19 pandemic on retinopathy of prematurity practice: An Indian perspective. Indian Pediatr 2020;57:979-80.
14. Kaur R, Sahan A, Thukral A, Chandra P. Impact of COVID-19 pandemic lockdowns on retinopathy of prematurity services at a tertiary eye care center in India. Indian J Ophthalmol 2021;69:2903-4.
15. Nair AG, Gandhi RA, Natarajan S. Effect of COVID-19 related lockdown on ophthalmic practice and patient care in India: Results of a survey. Indian J Ophthalmol 2020;68:725-30.
16. Mantagos IS, Wu C, Griffith JF, Jastrzembski BG, Gonzalez E, Goldstein S, et al. Retinopathy of prematurity screening and risk mitigation during the COVID-19 pandemic. J AAPOS 2021;25:e1-5.