Preferred practice guidelines for retinopathy of prematurity screening during the COVID-19 pandemic

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Abstract
Retinopathy of prematurity (ROP) is the leading cause of preventable infant blindness in the world and predominantly affects babies who are born low birth weight and premature. India has the largest number of surviving preterm births born annually. ROP blindness can be largely prevented if there is a robust screening program which detects treatment requiring disease in time. ROP treatment must be provided within 48 h of reaching this threshold of treatment making it a relative emergency. During the severe acute respiratory syndrome-coronavirus disease 2019 pandemic in 2020 ROP screening was disrupted throughout the world due to lockdowns and restriction of movement of these infants, their families, specialists and healthcare workers. The Indian ROP Society issued guidelines for ROP screening and treatment in March 2020, which was aimed at preserving the chain-of-care despite the potential limitations and hazards during the (ongoing) pandemic. This preferred practice guideline is
summarized in this manuscript.

**Key Words:** Retinopathy of prematurity; Screening; Preferred practice; COVID-19; Pandemic; Indian retinopathy of prematurity society

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**Core Tip:** Retinopathy of prematurity (ROP) is a relative emergency in ophthalmology because if it’s screening and treatment is delayed it can result in permanent vision impairment or even blindness in at risk infants. During the coronavirus disease 2019 pandemic, the Indian ROP society formulated these preferred practice guidelines with the aim of reducing this risk.

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**INTRODUCTION**

The severe acute respiratory syndrome-coronavirus disease 2019 (COVID-19) pandemic that started in the last quarter of 2019 in China and spread thereafter reached epic proportions globally by early 2020 and is still ongoing in most regions of the world. This pandemic has become the greatest public health calamity in over a century or more. Lives and livelihood were lost globally and sadly the true quantum of loss and the impact on the future health and well-being of the human race is yet to be fully determined.

At the time of this submission, India had the second largest number of cases in the world. Like most parts of the world, the Government of India (GoI) mandated the first lockdown of all non-essential services between March 25, 2020 to April 14, 2020, which was followed by a series of continual lockdown periods with differing restrictions.

Like all other healthcare specialties, ophthalmology was impacted tremendously. While routine daycare surgeries were suspended initially only emergency services were offered. Since ophthalmology is a stand-alone specialty with very few life-threatening or relatively fewer eye emergencies, most ophthalmology set-ups were shut down. Aiming to strike a professional and ethical balance between controlling the spread of the virus and providing services for ophthalmic emergencies, the All India Ophthalmology Society (AIOS) developed.

A preferred practice pattern (PPP) based on consensus discussion between some of the leading ophthalmologists in India, major institutional representatives, and the AIOS leadership[1]. The PPP was initially for the specialty as a whole and was applicable to all practice settings including tertiary institutions, corporate and group practices, and individual eye clinics. Subsequently, sub-groups developed practice guidelines for eye-banking, glaucoma, vitreo-retina[2], and pediatric ophthalmology.

Retinopathy of prematurity (ROP), a bilateral vasoproliferative disease affecting the retinae of premature infants within a few weeks of birth is a relative Ophthalmic emergency. As this affects the vulnerable cohort of infants during their critical admission in the neonatal intensive care unit (NICU), ROP screening and often treatment requires to be made available in the NICU itself by the ROP team. Even in pre COVID times, ROP screening in India is not universal, with an acute shortage of trained specialists to carry out the screening[3,4]. The COVID lockdown restrictions of admissions into these NICUs, cessation of public transport, the shutdown of routine outpatient services added to the woes of ROP screening and treatment in an already fragile situation.

On March 24, 2020 a day prior to the national lockdown, the Indian ROP (IROP) society, a professional body of ROP specialists published the preferred guidelines for ROP screening on their website[5], and subsequently a summary was published in the vitreo-retinal diseases preferred practice guidelines[2]. These guidelines were circulated to all its members and subsequently were used in other countries with similar demographic profiles in the South and South-East Asian regions.

**GUIDELINE METHOD**

The Executive Founder members of the IROP contributed to the formation of the guidelines[3]. The
paper was then compiled and reviewed by the entire committee. In case there was any difference of opinion, a mutual consensus was reached by discussion amongst all the experts. The final version of the document was approved by all the authors.

**Disclaimer by the authors**

These guidelines are not sacrosanct and may be customized and modified depending on the regional situation in a particular district, state, or country. These guidelines are also not permanent and may be updated periodically depending on the prevailing condition, existing regulations and national and international scenario. These guidelines are not to be regarded as medico-legal advice.

The guidelines are summarized below and pertain to screening and treatment of ROP.

**ROP screening criteria:** (1) Who? This remains unchanged from the existing National ROP Operational Guidelines (2018)[6]. Eligible babies include: Those born ≤ 2000 g grams at birth/those born ≤ 34 wk of gestation; and outside the criteria if requested by the treating neonatologist; (2) When? We must strive to complete the first screening before the baby is 30 days old. If possible high-risk babies (< 1200 g and < 30 wk) may be screened earlier between 2-3 wk of life; (3) Where? In the NICU if admitted. In the NICU or Ophthalmic Office if discharged; and (4) How Often? With the aim of reducing the number of screening visits and restricting them to have the highest yield of detection of vision threatening ROP, the following modification to the screening schedule is suggested: Screening for ROP was initially restricted to the compliance of the below GoI guidelines. At the time of submission of this manuscript, these no longer are mandatory, but are included here for historical importance (Table 1).

### CURRENT PREFERRED GUIDELINES-COMPLIANT WITH EXISTING RULES ON SOCIAL DISTANCING

Mother’s with their infants waiting for screening must maintain social distance while undergoing dilatation, screening or counseling.

Mother must place the infant on a designated cot with a plastic/polythene sheet/large newspaper, uncovers the face of the infant and step away more than 6 feet. The screener walks to the baby and screens (using indirect ophthalmoscopy or a retinal camera).

Do not screen if the baby has conjunctivitis. ROP screening can be deferred until the infection is settled.

The assistant or nurse (wearing face mask) may handle the head only if needed during the screening. After screening, screener must step back more than 6 feet. The mother then comes forward and picks up the baby and the ROP card with the findings documented.

The newspaper if used must be disposed in a yellow bin. The plastic/polythene sheet must be replaced or sanitized with an alcohol based sanitizer with a composition of, or similar to, a solution of liquid mixture of 1-Propanol and 2-Propanol (e.g. Sterillium or Bacillocid) before the next baby is screened.

Counseling the parents/other NICU staff must be done at a distance of 6 feet or more.

The designated cot must be sanitized using the above mentioned sanitizer. Other surfaces that may have been touched/handled by the physician/team/parent/must also be sanitized before the procedure is repeated for the next baby.

If an infant speculum is used during screening it should not be repeated unless sterilized before being re-used.

Eye drops used for dilating must be used carefully without touching the eye or eyelid and must be discarded at the end of the day or session.

The lens used for screening (20D or 28D) must be washed with water and soap and the rim should be cleaned with alcohol swabs. When a wide-field ROP camera is used, the lens tip should be cleaned with disposable alcohol swabs between each case.

Wherever possible, Personal Prophylaxis Equipment prescribed by the Indian Council of Medical Research must be used. The minimum protection that must be used by all members of the screening team are: Facial mask (preferably N95 grade), Head Cap, Eye protective glasses, Sterile gloves. However, these guidelines are constantly changing and the most updated recommendations must be followed.

Between each patient, hands must be washed and an alcohol based sanitizer as mentioned above must be used and allowed to dry before handling the patient.

The vehicle used for transporting the screening equipment are required to be sanitized every day before and after the screening sessions.

Tele-medicine must be encouraged. Tele-medicine platforms have been shown to be useful even in pre-COVID times[5,7].

To reduce the number of screening sessions, attempt must be made to pool infants of one district(s), region or center to maximize the efforts of the screening team.
Table 1 Mandatory questions that were required at the start of the pandemic in 2020

| No. | Before screening, as the following 4 questions: (as per Govt guidelines in 2020) |
|-----|--------------------------------------------------------------------------------|
| 1   | International travel in last 4 wk                                              |
| 2   | In quarantine period? (See stamp on hand or arm)                              |
| 3   | In isolation as some in family was COVID-19 positive or had contact with COVID positive patient |
| 4   | Fever, cough, cold                                                             |

If yes to any of these 4, the parent/guardian must not enter the hospital and screening will not be performed. These are applicable to the physician, care giver, screening team and hospital staff as well fever is also checked at entry point with a non-contact thermometer (false negative if anti pyretic is taken).

Table 2 Suggested follow-up schedule for retinopathy of prematurity during the coronavirus disease 2019 pandemic

| Finding in either eye with respect to zone | Next follow up | Comment                                                                 |
|------------------------------------------|----------------|-------------------------------------------------------------------------|
| Immature retina in zone 3 and zone 2 anterior | 3-4 wk or more | If the PMA is less than 34 wk/ < 1500 grams/sick and admitted infant, consider a closer follow-up |
| Zone 3 and Zone 2 anterior disease        | 3-4 wk         | Spontaneously regressing ROP can be watched                              |
| Zone 2 Posterior disease                  | 2 wk           | Unless associated with treatment requiring features (see below)         |
| Zone 1 disease                           | 1 wk or treat  | Have a low threshold for treatment                                       |
| Pre-plus                                  | Consider early treatment or early follow-up if pupil does not dilate well and media is not clear | Individualize for each case based on the tempo of disease and PMA |
| Pre-plus                                  | With good pupillary dilatation and clear media and other low risk features | Can delay the next screening by an additional 1 wk from the current guidelines |

PMA: Post menstrual age; ROP: Retinopathy of prematurity.

Outreach specialists must be implored to take on a larger role to perform screening in centers that are in their proximity. Image based documentation and additional opinion from senior specialists must be encouraged.

**Follow-up during ROP screening**
Follow up visits are an integral part of ROP screening. On the average each infant requires 3-5 screening visits before the retinae are mature or the baby requires treatment. During the pandemic, the attempt was to reduce the number of follow-up visits without jeopardizing the ocular condition. The aim was to ensure that the most critical disease would not be missed and would be picked up at the appropriate time to avoid delayed treatment and is summarized in Table 2.

**TREATMENT FOR ROP**
The gold standard for ROP treatment is laser photoablation. Anti-Vascular endothelial growth factors injected intravitreally are also used in certain cases. The impact of delayed ROP screening and treatment has been reported from a tertiary care center more recently[8]. The aim of these guidelines was and are to prevent such a situation by optimizing the timing and modality of treatment and is summarized in Table 3.

**Post treatment follow-up suggestions**
Follow-up after treatment can be done by outreach specialists wherever feasible or by the treating physician’s team if the former is not possible. The frequency of subsequent visits can be reduced and must be decided on case-to-case basis. Post intravitreal injection cases can be reviewed SOS/less frequently as normally followed in the initial phase. Recurrences can be addressed during the follow-up after the lock-down phase where possible.
Table 3 Suggested treatment guidelines for retinopathy of prematurity during the coronavirus disease 2019 pandemic

| Disease | Comment |
|---------|---------|
| Type 1 ROP (ETROP) [9] | Treat as soon as you possible, preferably on the day that screening was done. Laser recommended |
| AROP [10] | Treat as soon as possible. Laser if disease is amenable. Intravitreal injections can be used, but caution to be exercised since follow-up may be a critical issue with travel restrictions for the family |
| Less than Type 1 ROP, Stage 2 with pre-plus, stage 3 with no or early plus, high risk for APROP (but not yet full fledged), borderline Zone 1 disease/poor pupil dilatation, unclear media with pre-plus | Given the difficulty to closely follow-up consider treatment a ‘little earlier’ than classical Type 1 ROP |
| Stage 4A and 4B ROP [10] | Surgery must be performed as soon as treating ROP specialist feels it is required with adequate precautions taken while providing anesthesia |
| Stage 5 ROP [10] | Surgery is not urgent. Case-to-case based decision must be considered |

ROP: Retinopathy of prematurity; AROP: Aggressive retinopathy of prematurity.

CONCLUSION

ROP is considered a relative emergency in Ophthalmology and as ROP specialists we understand our duty and responsibility towards mitigating the risk of blindness in infants who are at risk of this disease.

However, these are not normal times. In this unprecedented time, it is imperative that we also do everything possible to minimize the risk of COVID-19 (Corona Virus) transmission to our patients and our staff while simultaneously engaging in treating and preventing vision loss in our babies.

These guidelines are not designed to be ideal. In a restrictive time that the country is facing due to the force de majeur condition that we have encountered, it is important to understand that ‘in good faith’ and ‘to the best of our ability’ should be the driving dictum of the ROP care. Our aim should be to reduce and mitigate blindness without risking the lives of our patients and our health care givers.

FOOTNOTES

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