# "A PROSPECTIVE CROSS-SECTIONAL STUDY TO DETERMINE THE PROPORTION OF RETINOPATHY OF PREMATURITY IN PREMATURE LOW BIRTH WEIGHT INFANTS OF ANEMIC MOTHERS"

By

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Dissertation submitted to

**SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, CENTRE, TAMAKA, KOLAR**

In partial fulfilment of the requirements for the degree of

**MASTER OF SURGERY**

**IN**

**OPHTHALMOLOGY**

Under the guidance of

**DR. B.O. HANUMANTHAPPAM.B.B.S., M.S.**

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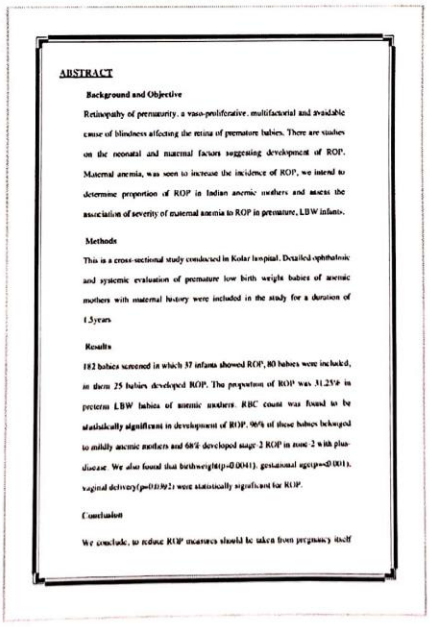

ABSTRACT

Background and Objective

Retinopathy of prematurity, a vaso-proliferative, multifactorial and avoidable cause of blindness affecting the retina of premature babies. There are studies on the neonatal and maternal factors suggesting development of ROP. Maternal anemia, was soon to increase the incidence of ROP, we intend to determine proportion of ROP in Indian anemic mothers and assess the association of severity of maternal anemia to ROP in premature, LBW infants.

Methods

This is a cross-sectional study conducted in Kolar hospital. Detailed ophthalmic and systemic evaluation of premature low birth weight babies of anemic mothers with maternal history were included in the study for a duration of 1.5years

Results

182 babies screened in which 37 infants showed ROP, 80 babies were included, in them 25 babies developed ROP. The proportion of ROP was 31.25% in preterm LBW babies of anemic mothers. RBC count was found to be statistically significant in development of ROP. 96% of these babies belonged to mildly anemic mothers and 68% developed stage 2 ROP in zone 2 with plus disease. We also found that birthweight(p=0.0041), gestational age(p=0.001), vaginal delivery(p=0.0392) were statistically significant for ROP.

Conclusion

We conclude, to reduce ROP measures should be taken from pregnancy itself

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# LIST OF ABBREVATIONS

| | |
|---|---|
| ROP | Retinopathy of prematurity |
| NFL | Nerve Fiber Layer |
| GCL | Ganglion Cell Layer |
| IPL | Inner Plexiform Layer |
| INL | Inner Nuclear Layer |
| OPL | Outer Plexiform Layer |
| PR | Photoreceptor |
| RPE | Retinal Pigment Epithelium |
| ONL | Outer Nuclear Layer |
| RGC | Retinal ganglion cells |
| PDGF-A | Platelet derived growth factor A |
| VEGF | Vascular Endothelial Growth Factor |
| RLF | Retrolental fibroplasias |
| $O^2$ | Oxygen |
| STOP-ROP | Supplemental Therapeutic Oxygen for Prethreshold ROP |
| RD | Retinal detachment |
| OCT | Optical Coherence tomography |
| CRYO-ROP | Cryotherapy for Retinopathy of Prematurity |
| ETROP | Early Treatment for ROP |
| D | Dioptre |
| NICU | Neonatal intensive care unit |
| ILM | Internal Limiting Membrane |
| GPCR | G-protein coupled receptors |
| WHO | World Health Organization |

| | |
|---|---|
| LBW | Low Birthweight |
| GA | gestational age |
| PVL | periventricular leukomalacia |
| BPD | bronchopulmonary dysplasia |
| NEC | necrotising enterocolitis |
| IVH | intraventricular drain |
| LIGHT-ROP | Light reduction in retinopathy |
| LIO | Laser indirect ophthalmoscopy |
| RDS | Respiratory distress syndrome |
| AC | Anterior chamber |
| EOM | Extra ocular muscles |
| BEAT-ROP | Bevacizumab eliminates the angiogenic threat of ROP |
| PMA | postmenstrual age |
| $CO_2$ | Carbon dioxide |
| GDM | Gestational diabetes mellitus |
| PPROM | Preterm premature rupture of membranes |
| WINROP | Weight Insulin-like growth factor, neonatal ROP |
| RBC | Red blood cells |
| MCV | Mean corpuscular volume |
| MCHC | Mean corpuscular haemoglobin concentration |
| MCH | Mean corpuscular haemoglobin |
| ICROP | International classification of ROP |
| ICMR | Indian council of medical research |

# ABSTRACT

**Background and Objective**

Retinopathy of prematurity, a vaso-proliferative, multifactorial and avaidable cause of blindness affecting the retina of premature babies. There are studies on the neonatal and maternal factors suggesting development of ROP. Maternal anemia, was seen to increase the incidence of ROP, we intend to determine proportion of ROP in Indian anemic mothers and assess the association of severity of maternal anemia to ROP in premature, LBW infants.

**Methods**

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**Results**

182 babies screened in which 37 infants showed ROP, 80 babies were included, in them 25 babies developed ROP. The proportion of ROP was **31.25%** in preterm LBW babies of anemic mothers. RBC count was found to be **statistically significant** in development of ROP. 96% of these babies belonged to mildly anemic mothers and 68% developed stage-2 ROP in zone-2 with plus-disease. We also found that birthweight(p=0.0041), gestational age(p=<0.001), vaginal delivery(p=0.0392) were statistically significant for ROP.

**Conclusion**

We conclude, to reduce ROP measures should be taken from pregnancy itself rather than after birth of baby, as retinal vessels develops in intrauterine period. Neonatal and maternal factors both are responsible for retinal development. Maternal anemia has risk of development of ROP and should be tackled aggressively as it may lead to blindness.



**Keywords:** Retinopathy of prematurity, maternal anemia, ROP, preterm infants, low birth weight.

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# INTRODUCTION

# INTRODUCTION

Retinopathy of prematurity(ROP), is a vaso-proliferative disorder in preterm babies affecting underdeveloped blood vessels of retina. It is a widely recognized as an avoidable cause of blindness in premature babies if detected early and managed as soon as possible.[1]

The exact pathogenesis of ROP is not fully known, numerous risk factors have been detected which contribute in increased frequency of ROP, the most prevalent risk factors being gestational age and birth weight.[2]

In India, approximately 110,000 preterm neonates survive every year due to advancements in supportive and therapeutic services for preterm in low to middle-income nations and therefore, increasing the risk of ROP.[3]

However, due to a scarcity of retinal examination-trained ophthalmologists, most preterm newborns, particularly those delivered and cared for in remote district hospitals, are either not checked at all or do not complete ROP screening.[3]

At present, screening guidelines are focused on 2 risk factors that is birth weight and gestational age by American Academy of Ophthalmology, and do not take into consideration the maternal factors which may also lead to the emergence of ROP.[3]

Some studies have indicated that maternal factors can also be a risk factor in retinopathy of prematurity.[2,4] They also suggest that maternal anemia is one of major risk factors for premature and low birth weight deliveries.[5]

Babies born to anemic mothers have higher chances of developing iron deficiency anemia with low hemoglobin count, serum iron and ferritin levels had higher chances of developing ROP.[2]

Hence with this background, we intended to draw a correlation between the proportion of development of retinopathy of prematurity in premature low birth weight babies of anemic mothers.

# AIMS & OBJECTIVES

# OBJECTVES OF STUDY

- To assess the proportion of ROP in preterm low birth weight babies with maternal anaemia.

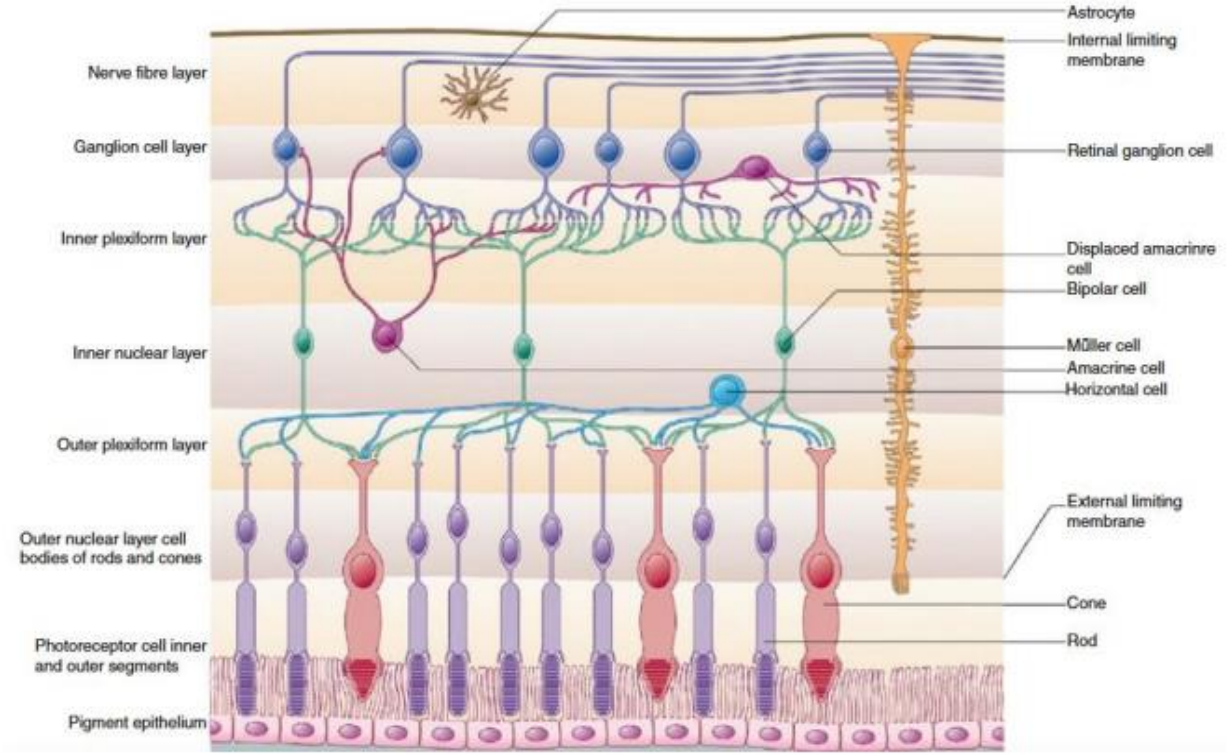
- To assess the association of severity of maternal anemia to incidence of ROP in preterm and LBW babies

# REVIEW OF LITERATURE

# A. RETINAL ANATOMY

All visual stimuli are communicated to the brain via a complex neurovascular organ called retina. Retinal architecture allows transmittance of light to photoreceptors and eventually to brain while the vascular network helps in keeping the tissue alive by supplying nutrients and gas exchange. The retina has 10 distinct layers[6], from the vitreous to the optic nerve comprising a diverse population of cells distributed in a specific manner as seen in Figure 1.

Fig 1: Layers of retina




## Layers of The Retina

Above figure shows retinal layers in order from top to bottom as follows:

(10) Inner Limiting Membrane(ILM)

(9) Nerve Fiber Layer[Nfl]

(8) Ganglion Cell Layer[Gcl]

(7) Inner Plexiform Layer[Ipl]

(6) Inner Nuclear Layer[Inl],

(5) Outer Plexiform Layer[OPL]

(4) Outer Nuclear Layer ONL]

(3) Outer Limiting Membrane

(2) Photoreceptor[PR]Layer

(1) Retinal Pigment Epithelium[RPE]

The **Inner Limiting Membrane** is composed of Müller cell's foot-processes which separate the retina from the vitreous body of the eye. The **NFL** comprises superficial vessels, astrocytes, microglia and the resident macrophages of the retina, that interact with the axons of the retinal ganglion cells (RGCs).

The nuclei of RGCs are in the **GCL** that interact with both astrocytes and Müller cells, the glial cells of the NFL, and synapse with amacrine and bipolar cells in the **IPL.** The **INL** therefore comprise of the nuclei of amacrine, Müller, bipolar, and horizontal cells that relay signals from the PRs to the RGCs.

In the outer segment layer **PRs** capture light through, and are separated from the **ONL** by the **Outer Limiting Membrane**. Light stimulates the PRs, they transmit signals to other neurons of the retina through synapses in the OPL.

Finally, the **RPE** borders the PR layer and sustains PR function by maintaining the constant renewal of their photo-pigments and by diffusing excess light that enters the retina.[7]

**Cells of the Retina**

It can be categorized into 3 main categories :(1) Vascular Retina, (2) Neural Retina, And (3) Glial Cells.

The **vascular retina** is comprised of vascular endothelial cells, pericytes, and smooth muscle cells that meet metabolic demands of the neural retina[8]; the neural retina comprises of cells that mediate visual function like RGCs, bipolar, amacrine, horizontal, and PR cells[9].

Vision is therefore primarily governed by the communication of multiple neurons, which in turn, are supported by the retinal vasculature. The glial cells mediate communication of both systems by exercising control over the extracellular environment.

The Photoreceptors are the dominant photosensitive cells in the outer retina that capture light through photopigments before signals are transmitted to the inner retina that harbour the RGCs.[10,11] The photopigments in photoreceptors are rhodopsin and cone opsin. Photoreceptors having rhodopsin are called rods and containing cone opsin is called cones. These photopigments respond to light by photoisomerization of G-protein coupled receptors (GPCRs). Signals are transmitted from photoreceptors and hyperpolarised membrane when light induces changes in conformation though interneuron synaptic connections and GABAergic neurons who refine and relay the signals to inner retina to RGCs in GCL. [12,13] Glutamatergic bipolar cells capture the synaptic output of PRs in the OPL and provide synaptic input to RGC and amacrine cells in IPL, they protrude up into the IPL and down into the OPL.[14]

Amacrine cells, like horizontal cells, function as negative feedback system to intra-retinal neurotransmission by communicating through GABAergic[15] and glycinergic signalling.[16, 17, 18] RGCs retrieve signals from amacrine and bipolar-cells at the IPL, and form the 2nd cranial nerve that communicates with the brain.[14]

Neurons in retina are responsible for neurotransmission whereas glial cells are important in regulating retinal function. They maintain retinal homeostasis. Retinal glial cells are the neurosupportive cells of retina that controls the extracellular environment to preserve neuronal function.[19,20,21]

The macroglia and microglia are the 2 types of glial cells; wherein the macroglia consists of Müller glia and astrocytes, and the microglia are the resident macrophages. The macroglia are mainly responsible for controlling the extracellular milieu by regulating blood flow,

maintaining the blood retinal barrier, removing debris, as well as managing interneuron communication.[22, 23, 24]

The Müller glia spans the complete depth of retina extending from inner limiting membrane to the outer and reinforces the structure of retinal tissue.[25] On the other hand, astroglia are only found in NFL, who govern the vascularisation of retina,[26,27] the fovea and Ora serrata are devoid of astrocytes as they are avascular regions.[28]

Müller and astrocyte cells act together to the needs of neurons, and maintain homeostasis in the retina by regulating levels of metabolic substrates[29] , potassium[30.31], glycogen[32,33] and neurotransmitters[19,20] that are important for neuronal function.

Activated microglia remove damaged neurons and synaptic connections by phagocytising debris. They respond only to stressors in the environment and remain dormant under physiological conditions.[23] Hence they are commonly regarded as resident macrophages that continuously survey the retinal milieu for signs of damage, inflammation, or infection.

**Vascularization of The Retina**

Vascularization in retina is considered to be driven by sprouting angiogenesis and partially by intussusceptive angiogenesis.[34]

It is believed that environmental cues are secreted by neurons and surrounding neuroglia towards which nascent vessels migrate, via chemotaxis.[35] Hence, the development of the retinal vascular bed is considered to be the product of intercellular cross-talk between the neurons, astrocytes, and endothelial cells of the eye.

The RGCs are the first to migrate from the optic disc towards peripheral retina to generate a radial framework formed by their axonal bundles; followed by astrocytes that are mediated by platelet derived growth factor A (PDGF-A) through communication with RGC. The RGCs release PDGF-A that stimulates astrocytic invasion as astrocyte expressing PDGF receptor (PDGFR $\alpha$) that follow the radial direction of RGC migration during development.[36]

Astrocytes enter the retina via 2nd cranial nerve and follow the RGCs to the peripheral retina and pave the way for vascularization. Endothelial cells follow the same migration pattern as neuronal and neuroglial cells after the appearance of RGCs and astrocytes. They help in providing a structural template for directing the retinal vascularisation by forming a framework for the migration of vessels. In physiological vascularisation, RGCs guide the development of growing vessels by releasing VEGF and other growth factors into the microenvironment thereby stimulating the immigration of endothelial tip cells and the growth of endothelial stalk cells that express VEGF receptors.[37]


Fig 2: Retinal vessel development at different months of gestation starting from 4th month.
Numbers refer to months of gestation, N= nasal retina, T= Temporal retina

Migration of vessels and vascular network is guided by VEGF produced by RGCs and with the help of astrocytes and endothelial cells through cell adhesion molecules; R-cadherin.[36]

Vascularization of the retina is complete when: vessels reach the periphery, excess vessels are pruned. Mural cells are recruited to reinforce the vascular structure.[38]

In humans, vascularization of retina starts at the sixteen weeks of gestation, and completes on term.[39]

## B. RETINOPATHY OF PREMATURTY (ROP)

ROP is retinal illness seen in preterm babies showing local ischemia with incompletely vascularised areas with subsequent retinal neovascularization. The disease spectrum varies from mild to advanced cases ultimately leading to irreversible loss of vision in both eyes.

### Historical Perspective

In 1942 throughout the developed world, ROP was first described and became recognized as the primary cause of childhood blindness.[40] It was originally called as Retrolental Fibroplasia (RLF) as per Terry's original reports, justified the fact that it occurred during progression of the embryonic hyaloids system,[41,42] whereas Owens and Owens[43] stated RLF developed postnatally and hyaloid system remained unaffected at birth.[43] In the later years after the diseases' course and signs became clearly understood, the term "retinopathy of prematurity" had been used.[43]

In 1950, the correlation between supplementary $O_2$ and ROP was discovered leading to a decrease in use of oxygen in the childcare centre leading to a dramatic reduction in ROP proportion.[44,45,46,47] Unfortunately, this also increased morbidity and mortality in infants.[48,49,50]

Nursery Practices in ROP

Arterial blood gas analysis has been one of the important modalities for assessing $O_2$

necessity in preterm babies with RDS.This discovery was introduced in the early 1970s which enabled pediatricians to maintain oxygen supplementation as per infant's oxygen needs.[51] Recently, neonatologists are able to monitor babies more intensively by using non invasive tools like modern transcutaneous oxygen monitoring and pulse oximetry. There are large multicenteric oxygen restriction trials suggesting lower range of target $O_2$ saturation (e.g., 85–89%) correlate with lesser chances of aggressive ROP but in return it also increases death rates.[52,53,54]

With advancements in neonatology, the most preterm newborn babies are now surviving. Survival of LBW infants has risen to 37-72% in 1950s with the help of ventilators, surfactant, intravenous nutrition.[55,56,57] Several collaborative randomized controlled trials have concluded that **prolonged duration of supplementary O2 is the principal cause of ROP**.[47]

In early 1950, several animal models were studied to know the progression of the disease and its association with O2 (Figure 3); it was suggested that immature retinas are more susceptible to oxygen toxicity causing greater risk of ROP development.[45,46,58]
Accordingly, it was also seen that in infants temporal retina is the last portion to vascularize and remains at risk for development of ROP for the longest (Figure 2)

**Oxygen supplementation on under-developed retina**

**First Stage of ROP (Vasoconstrictive and Vaso-occlusive stage)**

Raised blood oxygen in retina primarily leads to constriction of vessels by approximately 50% of the vascular caliber, in the next 4- 6 hours on continued oxygen exposure; gradual vasospasm is noted till the vessels are about 80% narrowed. In this stage, vasoconstriction remains reversible.[59] With time, certain immature retinal vessels in the periphery get

permanently occluded if the arterial oxygen partial pressure levels continue to remain elevated for an extra period of 10–15 hours.[46,60] With prolonged hyperoxia, the retinal occlusion progresses and leads to local vascular obliteration..[61] It is seen that there is hyperoxic damage selective to endothelial cells present in the immature retinal vessels.[62]

**Secondary Stage of Retinal Neovascularization**

It was seen that in animals, considerable amount of endothelial proliferation arises from the remnant vascular complexes beside retinal capillaries ablated during hyperoxia once subjected to ambient air; new vasculature formed from the proliferating endothelial cells canalize and proliferate inside retina and erupt the ILM to develop on its surface. This neo-vascularization is similar to other proliferative retinopathies. In some animals, the early preretinal neovascular formations were called 'popcorn' as they were similar to angioblasts with fewer lumens which mature into neo-vascular formations. This includes vessels invested with pericytes.[63,64] Preretinal neovascularization persists in dogs, results in tented membranes and traction retinal folds in the retina. [65] These preretinal neovascular structures in mice and rats regress after 5 days.[59,61,62,63,64,66,67,68] Capillaries tend to retreat from places with greater oxygen concentrations and multiply in areas with lower oxygen concentrations.

**Normal Retinal Vasculogenesis**

Michaelson originally suggested that optic nerve head has preexistent arteries and veins on the hyaloid vessels that give rise to retinal capillaries.[63] Cogan approved a mechanism that hypothesized solid endothelial cords proliferate from hyaloid vessels.[64] Mesenchyme was suggested to be blood vessel precursor by Ashton that grows towards the periphery of retina through nerve fibre layer from optic disc. A meshwork of capillaries called '**Chicken wire'** develops from the posterior edge of the advancing mesenchyme that undergoes absorption

and remodeling to produce mature retinal arteries and veins that is crowded by the capillary meshwork.[68,69] The key factor in guiding vascular growth is seen to be VEGF. This fits the description suggested by Michaelson's that is "Factor X."[63] It has been demonstrated in kittens, astrocytes are having a leading role in growth of capillary network by Chan-Ling and Stone.[70,71,72] Greater than 80% of preterm babies have noted to develop maturation of retinal vessels by full term.

ROP Pathogenesis

Previously, it was considered that "excess" oxygen was responsible for the earliest alterations in growing arteries. Studies conducted by Alon et al stated, hyperoxia causes VEGF downregulation and the reduction in number of endothelial cells, implying that VEGF is an endothelial factor of growth.[73] Following the completion of these emerging arteries, the separating retina becomes more pale and hypoxic, promoting VEGF overexpression and neovascularization.[71,74,75]

Szewczyk proposed hypothetically that increased oxygen ought to delay the arrival of such development factors and license neovascularization to redesign and relapse in a systematic style. Hence, he used oxygen to treat infants with significant ROP. From his report, a positive correlation was obtained but it was unclear whether the result was secondary to spontaneous ROP regression as there were no controls included in the study.[76]

A trial was conducted by the multicenter called as "**Supplemental Therapeutic Oxygen for Prethreshold ROP (STOP-ROP) trial"**, sponsored by the National Institute of Health headed by Dale L. Phelps, concluded that slight increase in oxygen saturation did not increase ROP once it was established, nor did it clearly benefit the ROP.[77]

The clinic-pathological and histo-pathological obsevations of Flynn and his companions [78-81] drove them to propose progression of ROP pathogenesis in humans:

1. Injury to Endothelium is seen where the primitive capillary meshwork is formed separating it from mesenchyme which was similar to animal studies in which capillary damage was restricted to the recently differentiated vascular complexes after a brief period of hyperoxia. At the moment, aside from oxygen environmental factors are considered to be involved;for instance, Nitric oxide was discovered to act on vessels playing a role in vaso-obliterative stage of ROP by Brooks and colleagues, [82] while Alon et al. discovered, endothelial cells may die when there is less VEGF because it is a survival factor.[73]

2. The matured arteries and veins formed from the mesenchyme survive this damage to the vascular endothelium and mix with the limited number of surviving vascular channels to develop a mesenchymal arterio-venous shunt that subsitutes the damaged or ruined capillary bed.

3. The avascular and vascularized retinas are separated by the mesenchymal arteriovenous shunt consisting of a nest of mature arteries and veins that are fed by primitive mesenchymal and maturing endothelial cells. In the vicinity of the shunt, there are no capillaries. This structure is considered as the pathognomonic lesion of acute ROP according to Flynn.[79]After the injury, Flynn described a period of days to months of dormancy in which no gross changes were noted in retinal findings. The shunt's tissues may become thicker; changing the structure's initial color from gray to salmon to red.[79]

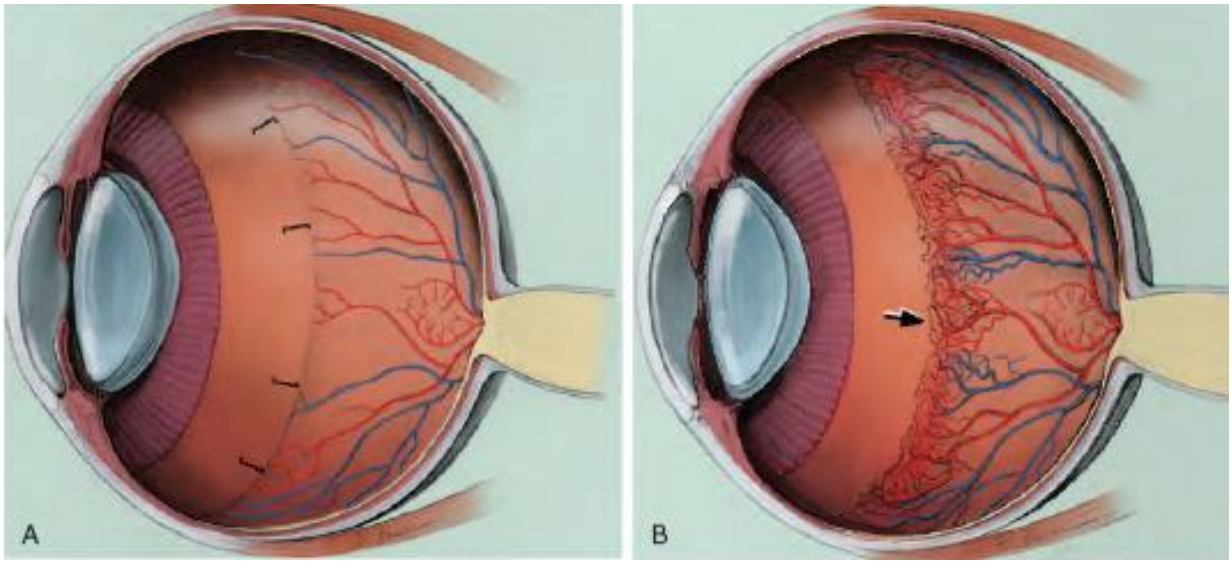



Fig 3:Fundus image showing retinal vasculature changes on exposing the kitten for short duration and longer duration of oxygen (a) it depicts the vascular closure of immature anterior retinal vessels in kittens when exposed to hyeroxia for short duration of time. Posterior retinal vessels remain unaffected. (b) Removal of the subject from hyperoxia to ambient air after 3

Flynn explained that primitive endothelial tubes with brush border of capillaries are spread towards the avascular retina anteriorly when the cells in shunts divide and become ordinary capillary endothelium. He found that involution of ROP occurred at the early stage in more than 90% of cases. However, as the disease progresses, the shunt's primitive cells proliferate and break through the ILM, expanding onto the retina's surface and into the body of vitreous. Flynn expressed: "The primary process of membrane proliferation results in traction detachment is due to lack of differentiation, destructive proliferation and invasion of cells into spaces and tissues where they are not appropriate."[79]

Foos suggested ROP pathogenesis primarily on histopathologic material examination.[83-85] He documented the phrases **"vanguard**" and "**rearguard"** to describe cell factors necessary for creating retina. The spindle shaped cells like glial cells form the Vanguard have a role in providing nutrition and oxygen to the immature retina for the duration of development, the

rearguard includes primitive endothelial cells.[86] As per Foos, when retina evolves, endothelial cells coalesce into cords and lumenize producing retina's primordial capillaries. 85 Neovascularization of ROP originates first from rearguard as well as primitive endothelial cells. He also stated that , after the expanding vasculature hits the anteriormost limit and develops, the spindle cells of the vanguard vanish. In their research, Chan-Ling[87], McLeod[88], and Provis[89] demonstrated that spindle cells seem to be endothelial progenitors that organise and mature to form the early retinal vasculature in foetal human and newborn dog retina.[87,88,89]

**Classification of ROP**

"**International Classification of ROP"** bifurcated retina into 3 antero-posterior areas and described the distribution of this disease by the 30 degrees meridians (Fig 5).

Stages of severity are documented on the descriptive changes in the retina and photographic standards.( Fig 4)[90]

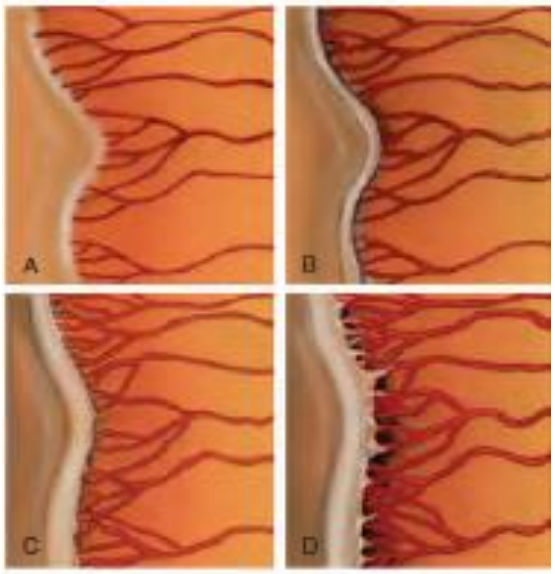



Fig 4: International classification of ROP. (A)Demarcation line, (B)Ridge(C) (D) extra-retinal fibrovascular proliferation mild and advanced stage respectively.

**Zones of Involved Retina**

The optic disc serves as the focal point for each of the three involved retinal zones (Fig. 5).

**Zone I** encompasses the posterior pole and is demarcated as a circle with a radius twice as great as the length between the opticdisc and the macula's center. It subtends a curve of around 60° (Fig. 5).

**Zone II** starts at the anterior limit of zone I and ends in a concentric circle that runs parallel to nasal ora-serrata. This boundary approximates the anatomic-equator in terms of time**.**

**Zone III** is the left out temporal crescent of the retina that is located anterior to zone II once the nasal vessels reach the ora serrata, it is the final area to become vascularized. This area is the most distant from the disc and is clinically critical to keep characterizing ROP as zone II in the event that there stays any dynamic ROP or juvenile vessels in the nasal retina.

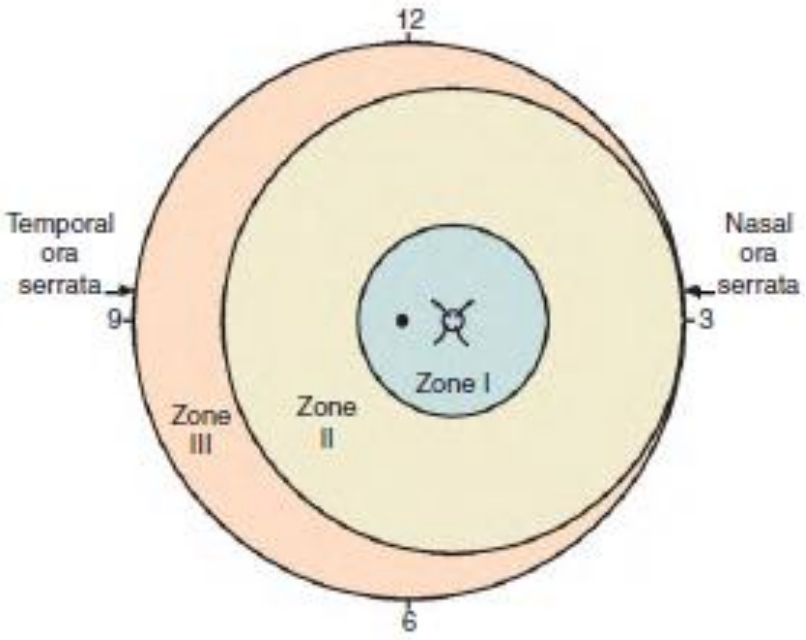



Fig 5: zones of retina as per ICROP

The actual diagnosis at the bedside can be subjective, particularly with regard to zone I. Because the fovea remains poorly defined in premature infants, the center of the macula is estimation. However, the definitions of the various zones are fairly explicit. Work by Chiang et al. showed that when 10 specialists checked on computerized fundus pictures, there was conflict in regards to which assessments showed zone I ROP in 33% of the cases.[91]

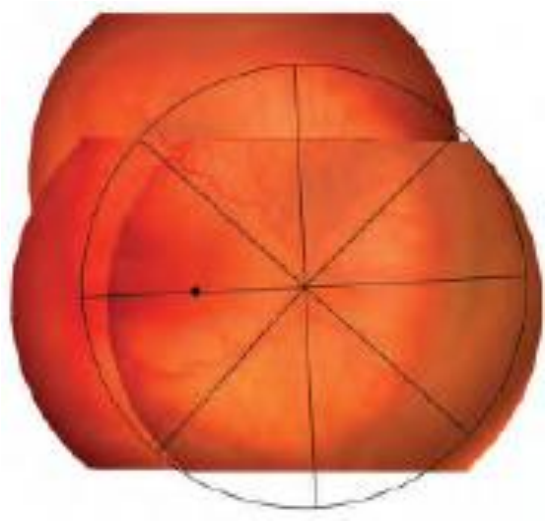


Fig 6: Retcam photo of the fundus depicting zone 1. Black dot represents the foveal centre

**Staging of ROP**

**Stage 1:** Demarcation Line: It is the first ocular sign of ROP that is seen in Stage 1 (Fig. 4 A). This structure distinguishes the posterior, vascularized retina from the anterior, avascular retina. It is white and flat, and it is in the retina's plane. The line is reached by vessels with abnormal arcading or branching. Stage 1 typically progresses to stage 2/involutes to normal vascularization within a few days, making it relatively ephemeral.

Garner and his collegues asserted that stage 1 demarcation line has been divided into two

separate areas. The more anterior vanguard area is made up of spindle-shaped cells that serve as the progenitors of differentiated endothelium of the vessels. As a result, it resembles the mesenchyme in its primitive stage (spindle cells) seen in normal fetal development but has significantly more cells. This demarcation line is made visible by hyperplasia, which involves both thickening and widening.[92]

**Stage 2:** Ridge: The demarcation line had evolved into a 3 dimensional slope that extends centrally around the the contour of the eye in stage 2. (Fig. 4 B). it might as well be whitish or pinkish and vessels might periodically leave the retina's base to enter it. Popcorn lesions represent tiny bundles of newly formed vasculature unattached to the posterior boundary of the ridge. This differs from stage 3 in the aspect that, there is no fibrovascular development on the ridge's surface. The proliferation of endothelial cells "with some evidence of organization into recognizable vascular channels" is what causes the stage 2 retinal ridge, according to Garner.[92]

On angiographic examination, Flynn and his colleagues demonstrated that the newly formed channels spill fluorescein at stage 2.[80]

**Stage 3**: It is distinguished by the presence of extra-retinal, growing fibro-vascular tissue from the preceding ridge (Figs. 4 C–D). This growing tissue is constantly confined by the back and inside section of the edge, resulting in a battered look of the rim as multiplication increases into the glassy. Similar to 2$^{nd}$ stage, vessels entering the ridge from the retina's surface could be misinterpreted for retinoschisis or even detachment. Although raised retinal vessels that extend from the base of the retina to the height of the ridge may not always suggest a detached retina, they can sometimes signal traction of viteous.[90]

Foos suggested that stage 3 "Extraretinal Vascularization" seemed pedunculated,polypoidal and placoid on histologic inspection. The most common and major pattern seems to be the placoid pattern, which is linked with the beginning of detached retina. Foos revealed that all these extraretinal vasculature seem to just be formed from multiplying endothelial cells instead of vaso-formative mesenchymal "spindle" cells using formulations of factor 8. Furthermore, he found considerable synchysis as well as vitreous body condensation in stage 3 depoly owing to hyaluronic acid merization and collagenous structure collapses into optically visible structures that are linked to vitreous condensation over the ridge.[85]

Diseases known as "Plus" and "Pre-Plus" disease denotes florid type of ROP. There seems to be vessel engorgement, dilation of iris and increased tortuosity of iris vessels, rigidity of pupils and hazy vitreous all show progressive vascular incompetence.

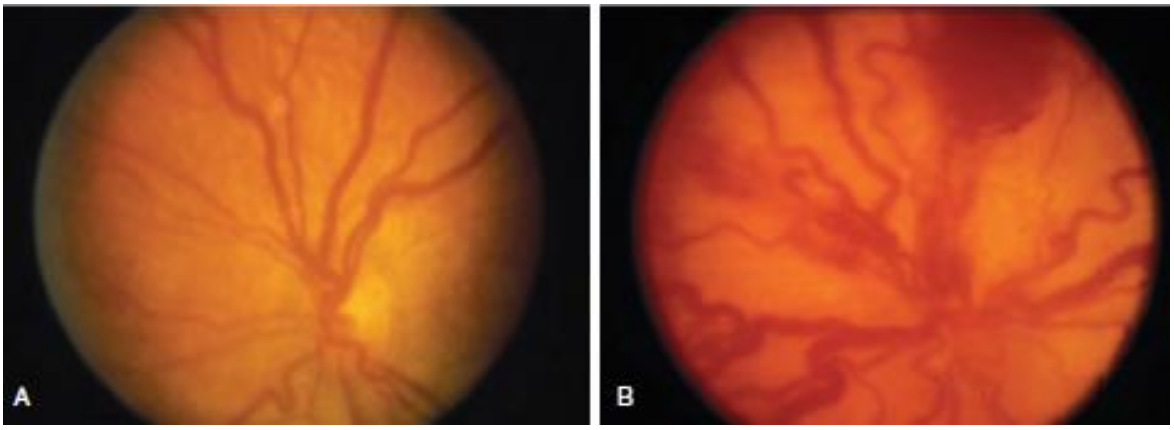



Fig 7: Plus disease. (A) Fundus photo showing dilation and tortuosity of vessels of retina and was seen in plus disease. (B) Fundus appearance of severe plus disease

When vascular changes are severe such that the arterioles are tortuous and veins are larger at that time a plus mark is added to the ROP stage. The minimal venous dilation and arteriolar tortuosity are necessary for plus disease and is represented by a published standard image

chosen by experts(Fig 7) and utilised in 4 multicenter clinical studies; this result is a crucial indication of a bad prognosis.[93]

“Revised International Classification” proposed "pre-plus" classification in 2005 as aberrant arteriolar tortuosity with posterior pole venous expansion, which is inadequate for diagnosing plus disease.[94] Centripetal growth from the ridge may develop almost concurrently with detached retina in severe plus disease in zone I. Since the growth indicating stage 3 may look fanned out "flat" rather than raised on the retina posterior to the ridge, ROP occurring in zone I may be critically deceiving. [67]

Flynn and Chan-Ling investigated the segregation between Zone I and Zone II ROP by distinguishing between vasculogenesis, which occurs when vascular precursor cells transform into new vessels, and angiogenesis, which occurs when existing vessels are regenerated. The authors hypothesized that because VEGF is not involved in the disease mechanism, zone I ROP is less responsive to laser treatment or cryotherapy. Hypoxia-induced VEGF-165 mediates angiogenesis in zone II ROP, making it more responsive to laser or cryotherapy treatment.

**Aggressive Posterior Retinopathy of Prematurity, is** known as "rush disease" an uncommon, severe form of ROP as per the “Revised International Classification of ROP” in 2005. There are several characteristics that distinguish this rapidly progressive variant of the disease: it occurs in zone 1 or posterior zone 2, the peripheral retinopathy is ill-defined, and the plus condition is disproportionate to the peripheral findings. There is no need for serial evaluation to diagnose this condition as it might/ might not progress through stages 1–3.Diagnosis can be made with only one assessment and without any sequential evaluations. In

reality, the disease displays at the junction between the vascular and avascular retinas as a flat area of neovascularization.[94]

**Classification of RD**

A second international committee of ophthalmologists and pathologists was established in 1987, expanded the international classification that was established in 1984 to explain morphology, location, and extent of retinal detachment(RD) (Fig. 8).[95] This classification is determined by pathologybased knowledge of how severe ROP develops and surgical experience.[85] Stage 4 (subtotal) RD, is typically tractional uplifted retina with findings in stage 3, at times exudative effusion is seen in stage 3 from adjacent neovascularization, when the disease is active.

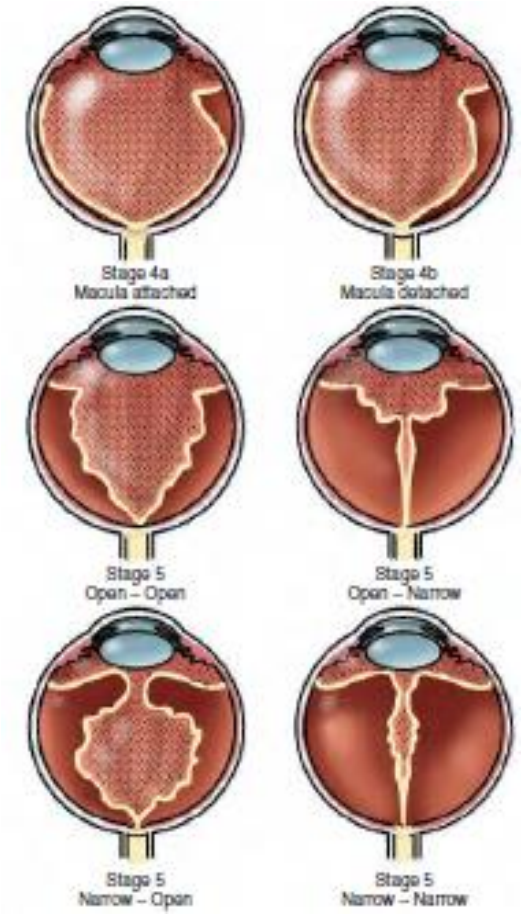



Fig 8: Retinal detachment configurations in ROP

**Stage 4A: Extra-foveal Retinal Detachment**

The central macula is typically unaffected by this concave traction detachment in the periphral retina( Fig. 9). Typically, vitreous traction and extraretinal fibrovascular proliferation are whe re these detachments take place. Elevation can progress from

any area where stage III disease has partially regressed and can become circumferential after ablative treatment with laser/cryotherapy.

They can be segmental present only in one portion of the periphery, or they can extend all the way around the periphery without elevating the macula. When no posterior extension is present, the anatomical and visual prognosis is fairly favorable.

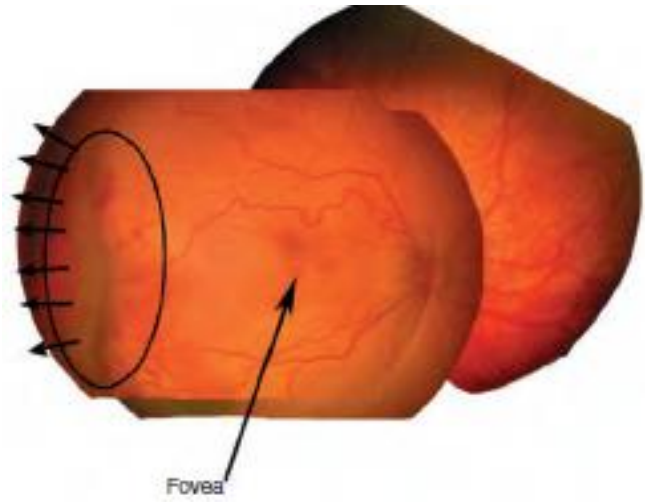



Fig 9: Fundus photo showing Stage 4A ROP in right eye. This photo shows retinal elevation posterior to the partially involuted Stage III ROP. Arrows indicate vitreous traction and oval area indicates possible area of RD

**Stage 4B: Partial Retinal Detachment Including the Fovea**

This follows as a continuation of stage 4A and may appear as a fold from the disc extending from zone I to II and III (Fig. 10). The prognosis of visual recovery is poor once detachment includes fovea in stage IV.

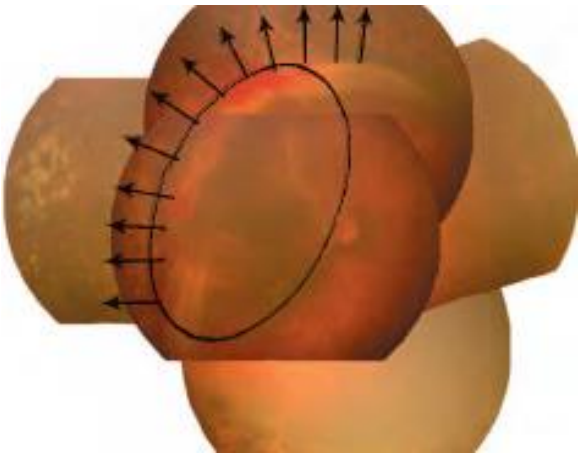


Fig 10: Fundus photo showing Stage 4B ROP in right eye;elevation of retinal area posterior to fibrotic ridge of partially involuted stage 3 ROP. Vitreous traction is shown by arrows, oval area shows possible area of RD.

**Stage 5: Complete Retinal Detachment**

It is shaped like a funnel, divided into an anterior and posterior section by stage 5 detachments (Fig. 8). The funnel is like an elective setup in which the channel is limited on both ends. The disengaged retina has been found simply posterior to the focal point. A 3$^{rd}$, lesser common type has the funnel open in the front but narrowed in the back. A funnel that is narrow at the top and wide at the bottom is the least common.

**Other Factors Related to RD**

The clinical features in stages 4 and 5, are the focus of the classification of RD in ROP:

1. The Retrolenticular Space's appearance. Translucent tissue that has been extensively vascularized may occupy this space, indicating disease activity. The tissue in this space turns white and lacks blood vessels as the disease goes away. This characteristic appearance has given rise to the terminology "retrolental fibroplasia".

2. Peripheral trough-it is indicated by an attached/shallowly detached stretched, avascular and non-functional retina l periphery seen as a lateral red reflex in conjunction with apparent narrow funnel stage 5 RD.

3. Anterior Segment changes seen are:

a) Edema of the cornea and a shallow AC; of the eye might be a typical early sign in preterm babies; however, it is a serious consequence in combination with RD in ROP.Corneal decompensation, flat AC and Acute angle closure glaucoma may develop sometimes.

b) Abnormality in the iris; posterior synechiae is a common finding in stage 4 and 5 ROP as well as ectropion uveae and iris atrophy. Attachments towards the anterior capsule of the lens, as well as the presence of the pupillary membrane with it's own preserved vascular network, can drive the iris to stiffen, especially in individuals with stage 5 illness. The pupil may seclude on occasion, resulting in iris bombé and angle closure.

4. Subretinal blood and exudates can be distinguished by Ultrasonography and OCT, but it might be challenging to do so. Fibrotic membranes under the retina might be present, but they have been typically discovered only during surgery.

**ROP in involution**

ROP involution often starts at 38weeks post-menstrual age and is characterized by a reduction in staging/development of vessels of retina in the peripheral zones.[96]

**Regressed ROP: RD, Squint, and Amblyopia**

While acute ROP frequently regresses without developing into RD, its sequelae can persist. After ROP has run completed its course, the eye is in a reasonably stable state known as regressed ROP.[97,98]

The residual changes in Table 1 have been distinguished into those that affect the posterior fundus and those that affect the retinal periphery. Pigmentary changes in retina may be mistaken for treatment side effects. RD and angle closure glaucoma are the late complications that develop in regressed ROP.[99]

Retinal separation can occur at any time after the neonatal period, yet particularly quite a while after birth, occurs as a sequelae from ROP. Retinal breaks and detachment are more likely to occur in eyes with short sightedness, retinal peripheral pigmentary changes or lattice like degeneration, changes at the vitreoretinal interface, condensation of vitreous and folding and stretching of the retina. Eyes with fractional retinal separation present at around 90 days after limit retinopathy stay in danger for movement of the detachment.[100]

**Table 1: Regressed ROP**

| **Peripheral changes** | | **Posterior changes** | |
|---|---|---|---|
| **Vascular** | **Retinal** | **Vascular** | **Retinal** |
| Abscence of vascularization of the periphery of the retina (Non-dichotomous, abnormal branching of retinal vessels, circumferential vascular arcades have interconnections and Telanglectatic vessels) | Pigmentary retinal changes, changes in Vitreo-retinal interface, Thinned out retina, Vitreous membranes with/without attachment to retina, Lattice-like-degeneration, Retinal breaks and folds, Traction/rhegmatogenous RD | Tortuous vasculature in the temporal arcade, Abnormal widening or narrowing of major temporal arcade occurs at the angle of insertion | Pigmentary changes ,Distortion and ectopia of macula, peripheral vitreo-retinal interface changes secondary to folding and stretching of retina in macular area. |

By and large, visual results for 61 eyes considered were poor: Parents should be made aware of the signs of RD and educate the child as soon as they are old enough to recognize and

report them. Only six eyes had visual acuity greater than 20/200.[100]

At the three month follow-up assessment in "Cryotherapy for Retinopathy of Prematurity (CRYO-ROP)" research, 6.6% of newborns weighing 1251 grams at delivery were diagnosed with strabismus. Patients with regressed Retinopathy of prematurity are more prone to acquire deviation of the eye and amblyopia. At three months, strabismus was significantly predicted by the presence of ROP. Subgroup analysis showed that the chances of deviation of the eye elevated as the stage and zone of ROP got worse.[101]

All infants with ROP should have regular eye exams for assessing refractive and EOM status until they are about 18 months old, or as long as it is clinically necessary. At corrected age of 24 weeks, 20% of babies with high risk pre-threshold ROP as well as 10% of newborns with low risk pre-threshold ROP exhibited strabismus in the multicenter "Early Treatment for ROP" (ETROP) research. Ophthalmic surgeons are educated about the awareness of substantial diversity in ocular position in newborns with a history of active ROP. At 36 weeks corrected age, 30% babies with highrisk pre-threshold ROP had squint.[102]

**Ocular Signs in Regressed ROP**

Refractive errors

20 % of infants in CRYO-ROP study who had a birth weight of less than 1251g were found to have shortsightedness within the first two years of life stating that myopia is more likely in babies with low birth weights. Myopia prevalence increased in ROP infants and is in direct correlation with ROP severity. For instance, 44-45 percent of individuals with zone II stage 3 ROP(no plus disease) had shortsightedness at 12 and 24 months postpartum. According to the ETROP trial, babies treated for high-risk pre-threshold ROP had 58% myopia at 24 weeks

post-term, 68% myopia at 36weeks post-term, and no improvement afterwards until 3years postnatal age.[103]

In addition, babies in this birthweight group with no ROP had a rate of 13% shortsghtedness. Between the ages of six months and three years, shortsightedness steadily raised. There had been minimal difference in the incidence of shortsightedness in eyes of zone I/ II ROP, and between plus and no plus disease. Shortsightedness was more common with persistent ROP (temporal straightened arteries or macular heterotopia).[104] Precise cause of shortsightedness is still unknown. According to Fletcher and Brandon, shortsightedness may occur secondary to the result of stretching of the eye, the lens or corneal curvature variations, or at times combination of these things.[105]

Patients with regressed ROP are more likely to have astigmatism and anisometropia. In CRYO-ROP study, 3.3% of 2518 babies born at 12 months weighing less than 1251g post term had anisometropia. In ETROP study, 401 infants with pre-threshold ROP were randomly assigned to conventional treatment or early treatment (laser photocoagulation at high-risk prethreshold ROP) in the event that threshold ROP developed. At 6months, 9months and 2years and 3years of age, respectively, all infants were refracted. The early treatment and conventional treatment groups had similar rates of astigmatism at each test age. Astigmatism was found in 42% of both groups at 3 years, up from 32% at 6 months.[106]

About 20% ROP cases are not symmetrical, when they touch threshold for treatment, these variations may have contributed to anisometropia. Amblyopia, nystagmus, and squint.[107,108,101,109]

Cornea and Lens signs

In CRYO-ROP study, the incidence of cataract was 0.3 percent at 12-month examination. Lens opacification or no lens was observed in 4.9% of early managed eyes and 7.2% of traditionally handled eyes in the ETROP study's final 6-year assessment of 271 children with symmetric ROP.[110] Kushner noted that vision is severely deteriorated in cases of early development of cataract with presence of retinal abnormalities.[109] Adults with pre-existing ROP can get good results from cataract surgery.[111] Patients with ROP are also more likely to get band keratopathy, acute hydrops, and corneal curvature irregularities.[93]

**Glaucoma in ROP and Regressed ROP**

Later in life, retinopathy patients may develop acute or subacute glaucoma. During the first six years of life, 1.67 percent of the enrolled eyes in the ETROP Study developed glaucoma. This was linked to a shallow chamber and retinal detachments of stage 4B or worse.[112] Parents should be taught to seek advice from ophthalmologists if they notice signs of hazy cornea and episcleral injection. In appropriate cases of glaucoma with ocular damage from ROP, a test was conducted to assess the effectiveness of steroids and cycloplegic drugs used topically with add-on anti-glaucoma medications may be required.[113]

Even in adulthood, eyes with regressed ROP are more likely to develop acute angle closure glaucoma.[114,115] Kushner noted that few individuals with minimal clock hours of regressed ROP had more chances to develop glaucoma.[113] As certain kinds of glaucoma might very well be treated surgically in some situations, ophthalmic surgeons and patients are educated about the potential consequences, related signs and symptoms and how to manage them.

**Examination timing**

The CRYO-ROP study's nursery surveillance yielded confirmed info regarding the initial stages of ROP. They found that ROP begins at a definitive schedule based on the babies's corrected age, also known as the postconceptional age, instead of chronological age, which is the time since birth.[116]

**Screening Guidelines**

An established regulations have been preferred for assessing preterm children during that period to detect the onset of advancing ROP and especifically development of pre-threshold ROP, which is explained as ROP of lesser severity than the threshold severity in CRYO-ROP trial. This is due to the fact that ROP may progresses to blindness at the first 12weeks of life and that therapy is available to halt it in most of the cases, especifically any stage 2+ or stage 3ROP in zone I, zone II, or both, with or without plus disease.[116] The American Academy of Ophthalmology and Pediatrics currently recommend a screening program for ROP in babies born on or before 30weeks or weighing <1500 grams. Children born between 28-32 weeks gestational age should have their initial examination four weeks after delivery, and those born on or before 27 weeks should have at 31 weeks. [117]After 45 weeks of gestational age , the chances of developing visual blindness secondary to ROP reduces if the baby has not developed any prê-threshold ROP or worse until then.[118] This information is exclusive for babies born in the United States and the course of ROP might vary in different areas of the world.

Side-Effects of Examination

Exceptionally LBW babies, are at a very vulnerable stage and should be examined with care. An Indirect ophthalmoscopy is deemed necessary when there is a probability of treatable

disease to progress to irreversible blindness or when data is required to assist in the general medical evaluation.[119]Screening regimes need to be developed keeping in mind that the events during the screening may be stress inducing for the baby.

Procedure of Eye Examination

An attending neonatologist should either ask for the exam or give the go-ahead to conduct it. In most newborns, cyclopentolate 0.2% and phenylephrine 1% eye drops can successfully widen pupils. To prevent systemic adverse effects such as high blood pressure and intestinal ileus, the remaining droplets are quickly wiped away from the lids.[119] Mydriatic drops can be replaced with 0.5% cyclopentolate, 1%tropicamide, or both, and 2.5%phenyl-ephrine can be given twice to children with darker complexion. After around twenty five to thirty minutes, the procedure has been performed using an ophthalmoscope(indirect) and condensing lens. The majority of examiners utilise a lid speculum, in which there are several acceptable for preterm newborns (like: Barraquer, Sauer, Alfonso specula). The inspection is frequently assisted by a nurse, and the baby's hands should be physically restrained. To avoid viral/chlamydial contamination, the eyelid speculum for every newborn must be clean, the inspection lens should always be cleansed with a spirit sponge between patients anytime it comes into contact with the infant's face. As a normal precaution, gloves should be worn during the inspection.[116]

If ROP is very severe, it will be typically be visible in the posterior aspect of the fundus without scleral indentation, but serial evaluations past fullterm or, atleast until the retinal vessels grow upto the nasal end of ora serrata is necessary to determine whether vascularization has advanced into zone III.[95,116]Scleral indetation is done by may be accomplished with a low-cost, sterile, and relatively mild "Calgiswab" nasopharyngeal

culture swab. The tip maybe twisted to any angle you wish, to resemble a tiny muscular hook. Scleral depressors for baby exams like the Flynn depressor are also available on the market.[116]

Most of the time, topical anesthetic like proparacaine is used to treat scleral depression. A member of the childcare staff should be available throughout the evaluation to deal with apnea or other potentially harmful reactions, as well as to monitor the child's breathing, vitals and behavior.

**Counseling of Patient's family**

It is seen that as the baby reaches medical stability ROP becomes severe which makes it challenging for parents. The results of eye exams should be communicated to families by the ophthalmologist or neonatologist. The Ophthalmologist should counsel the parents about any progression in the course of disease and especially inform them when ROP develops in zone I/II ROP reaches stage 3. Regularly informing the guardians will lessen the emotional impact in the event that the ROP damages the child's vision and also paves the way for discussing any possible intervention.[116]

**THERAPY FOR ROP**

Vitamin E uses:

Due to its antioxidant properties, vitamin E was thought to be an option for ROP prevention. It was assessed by Johnson et al.[120,121]with ensuing controlled clinical preliminaries playing tried the part of huge portions of nutrient E. [122-128]The outcomes were dubious and a report from the Establishment of Medication distributed in 1986 closed: "An in-depth investigation was conducted on the use of vitamin E as a preventative for retinopathy of prematurity.

Vitamin E consumption did not appear to be either beneficial or harmful, according to this committee's findings. Vitamin E appears to pose very little risk to preterm babies, if the doses are kept to a minimum of 3 mg/dl in the blood."[129]At present, no proper suggestion is there on the utilization of vitamin E in ROP.

The Role of Light

Terry considered premature eye exposure to light as a significant etiologic possibility in his initial descriptions of RLF.[130] Two studies investigated the effect of light before the importance of externally supplemented oxygen levels in ROP was recognized. Hepner and his colleauges[131]patched eyes of 5preterm newborn from birth until their weight reached 2kg in the late 1940s. They discovered that four of the five newborns had ROP and suggested that light had no influence in its genesis. Locke and Reese covered a progression of 22 premature newborn children (birth weight < 2kg) in 1952, in which they treated one eye of each kid.[132] A feasibility experiment of reducing light sunglasses (LIGHT-ROP research), headed by James D. Reynolds, and financed by National Eye Institute in 1995 at 3 childcare facilities in United States, revealed significant change in the frequency of ROP between covered and uncovered eyes.[131,132]

Half of 409 newborns with birth weight <1.25 k g were selected randomly to either put sunglasses having 97% near-neutral density filters till 8 months after conception or not get any exceptional light restriction. The experiment suggested that light had no clinically meaningful influence on beginning or severity of ROP.[133]The American Academy of Ophthalmology and Pediatrics had developed no guidelines for minimising the quantity of ambient light that gets into preterm newborns' eyes.[133]

Cryotherapy

Since 1968, reports have suggested that premature infants with ROP may benefit from a more manageable course of the disease if the peripheral retina is ablated. The initial reports suggested that cryotherapy or photocoagulation could accomplish this objective. Cryotherapy's efficacy and role in severe ROP was the subject of contradictory research beginning in the early 1980s,[134-139]highlighting the need for a multicentric clinical trial.[133,140-143]

In 1985, The Cryotherapy Multicenter Study made Earl A. Palmer in charge of organizing the CRYO-ROP study; it began by enrolling premature infants weighing <1.25 kg at birth in 1986, financed by the National Eye Institute. CRYO-ROP trial was analyzed by using a blinded comparison of fundus images of occurrence of clinically apparent folds of macular, detached retina, or retro-lental mass in eyes that underwent cryo-therapy against those that did not.[144]

Cryotherapy had been observed to lessen adverse fundus outcomes throughout the course of the serial evaluations. Babies having ROP of stage 3 in ≥5 meridians of retina posterior to zone 3 in the context of standardized plus disease have been deemed suitable for cryotherapy. At the 10-year evaluation, 27% negative fundus findings were obtained in eyes that underwent therapy against 48% control eyes, and visual acuity was found to be ≤20/200 in 44% of operated eyes vs 62% of controls..[144]

**Treatment Techniques in ROP**

In CRYO-ROP trial, 50 individual freezes were used on an average. When explaining the method of analgesia or anaesthesia, the external provisions of the childcare centre, accessibility to operating and procedure cubicles, skills of anesthesiologist, current clinical

stability of the baby, the baby's "track record" of enduring prior strenuous tasks, skills of cryosurgeon, and posterior limit of ROP all are taken into consideration..[133-143]

Laser Contemplations.

At the beginning of the 1990s, recognition was granted to laser ablation as a substitute for cryotherapy. Ophthalmic sugeons have established that LIO delivery technique is technically simpler to perform than cryotherapy and is associated with milder post-op problems such as oedema and inflammation. In 1990s, w hen LIO delivery devices were first introduced, the only laser provided had been an Argon Photo-Coagulator (488–532 nm). Furthermore, it became clear that the effects of treating threshold ROP in zones 1 and posterior edge of 2 were preferable to cryotherapy, and the outcomes were comparable to the treatment done by cryotherapy in zone 2 ROP.[145-154]

The diode laser photocoagulator (810 nm) was then introduced. Large spot laser indirect headsets followed, offering a 3-fold raise in the area covered by a single spot.

The infant is wrapped in a blanket and placed in an open warmer for laser treatment in the NICU. A neonatal nurse assists in the administration of mydriatic drops and treatment. In the event that resuscitation is required, a neonatologist must always be present in the nursery. Throughout the procedure, a pulse oximeter, apnea monitor, and heart rate monitor are utilized. A lid speculum is inserted and topical anesthesia is injected into cul-de-sac of eye(s) to be treated. For local anesthesia, 2% licocaine is injected subconjunctivally (0.25–0.3 ml) into each quadrant which takes 10minutes to act. Treatment is then started with the LIO, Proper laser wellbeing precautionary measures should be taken for the insurance of all faculty included.

To limit the skip lesions, burns caused by photocoagulation, they are conveyed in a confluent pattern to the entire peripheral nonvascularized retina as part of the treatment. A Calgiswab and sclera depressor are utilised for proper alignment the eye, treatment is typically initiated at the vascularised anterior edge of retina and applied to ora serrata. The diode lasers' initial settings include pulse duration of 0.3–0.4seconds and a power of 0.2 W. Until a yellowish gray burn is obtained the power is titrated, which is typically below the threshold for photocoagulation. In avascular retina, the power and duration are frequently changed from 1 area to another.

The size of the eye's avascular zone will primarily determine the total number of laser treatments required to treat that eye. According to the authors' experience, one thousand spots of laser might be enough to cover the avascular retina completely if ROP is located in middle to peripheral of zone II. However, if affected eye to be treated only has vessel growth in zone I, thousand five hundred to three thousand spots of laser may be applied for adequate coverage. In the event of a post laser hyphema or bleeding of vitreous that would reduce subsequent treatment, laser is typically performed in one session. However, there may be circumstances that require multiple treatment sessions, like decreased visibility or distress. In the absence of involution, occasionally missed areas near the ROP ridge necessitate additional treatments of laser.

**"Early Treatment for Retinopathy of Prematurity Trial(ET-ROP)"**

Under the orders of William V. Good, the National Eye Institute supported a trial in 1999 to investigate the most effective ROP treatment. In ETROP study, when an eye reaches a highrisk level of pre-threshold ROP, it was randomly assigned to either traditional treatment (only to observe and not to intervene until threshold ROP criteria have met) or early

peripheral retinal ablation. Unfavorable visual acuity results had been minimized by early intervention to 14.5% in selected high-risk eyes and from 19.5% in traditionally treated control group(p=0.01), by measuring the visual acuity outcome at a corrected age of nine months and structural conclusion of the retina at corrected ages of six and 9months.[155]In early treatment eyes, negative structural outcomes decreased from 15.6% in the control group to 9.1% (p.001).

| **Table 2: Indications of treatment(ETROP)** | |
|---|---|
| **Type I ROP** | **Type II ROP** |
| Ablation done to the periphery | Observation of the progression |
| Zone 2:Plus disease with stage 2/3 | Zone II: Stage 3 with no plus disease |
| Zone 1: Plus disease with stage 1/2/3<br><br>Stage 3 with no plus disease | Zone I: Stage 1/2 with no plus disease |

As shown in Table 2, the findings of the ETROP trial, released in 2003 December, resulted in the creation of a brand-new clinical algorithm that serves as a protocol for the management of eyes with severe ROP.[155] Eyes with type 1 ROP are recommended to receive prompt treatment, while eyes with type 2 ROP are recommended to continue making serial observations without receiving treatment. ETROP trial warns, plus disease must enlarge and twist the blood vessels of retina posteriorly as they exit the optic nerve in at least two quadrants (typically ≥6 clock-hours), achieving the published standard

Early therapy decreased unfavourable visual outcomes with type 1 ROP from 32.8% to 25.1% in the traditionally managed control group at the last analytical outcome tests done at age six (p=0.02). In the early treatment babies, unfavourable visual acuity outcomes climbed to 23.6 % in comparison to 19.4% in traditionally treated group with type 2 ROP.[99]This

difference, however, wasn't significant statistically(p=0.37).[155]

Only 66% of high-risk eyes chosen at random for conventional treatment in the ETROP trial received laser therapy(cryotherapy was rarely used). In comparison to the machine-generated algorithm that was used to acquire research subjects for the study[156], secondary analysis of the extensive data resulted in a simplified update of the treatment (Table 2).

If newborn eye exams are not performed, as was the case in the ETROP study, some of the benefits of a policy that prioritizes earlier treatment may be lost. A careful examination of methods used in the trial [157]reveals a big result on the policy for serial ROP examinations in an intensive care unit. As a result, take into consideration the following schedule for infants who do not meet the treatment guidelines;[117]

• **≤1 week follow-up for ROP type II:** Zone II stage 3 and no plus; Zone I stage 1 or 2 and no plus

• **1–2week follow-up:** Zone 2, without plus, stage II; Zone 1, immature, no ROP; Zone 1, ROP involution

• **2-weeks followup:** Zone 2, without plus, stage 1; Zone 2, ROP involution

• **2–3week followup**: Zone 3, without plus, stage 1/2; Zone II, immature, without ROP; Zone 3, ROP involution.

Reaching the post-conceptual age of 45weeks without having type II ROP and either finishing complete vascularization of retina or advancing into zone 3 without prior zone 2 ROP are both positive indicators of ROP advancement or regression.[118]

**Anti-VEGF Therapy for Posterior Retinopathy of Prematurity**

In adults, Bevacizumab's is beneficial if used in wet age-related macular degeneration due to presence of choroidal neovascular membranes. This has been demonstrated in numerous studies, they have expressed an interest in applying this experience to treatment of active ROP. The BEAT-ROP research, it was a multicenter prospective research, in this 150 newborns with ROP in stage 3+ in zone I/II in both eyes had been randomised to undergo bevacizumab intravitreal(0.625 mg) or traditional laser therapy. Multiple r ecent case studies, have found that anti-VEGF antibody intravitreal injections, like bevacizumab, is an extremely promising alternative for severe ROP. [158-163]

This study found that children with stage 3+ disease in zone 1 managed with bevacizumab had considerably lesser relapses and improved outcomes than babies with posterior zone 2 ROP at 54 weeks postmenstrual age.[164]More specifically, 6% of children with zone 1 treatment-requiring ROP required additional treatment. Contrarily, additional treatment was required in 42% of the laser-treated eyes. It is important to note that the unfavorable structural outcome in the ETROP study was only 22.2 percent for zone II with plus and no stage 3 and 29.6 percent for zone I with stage 3 and/or plus.

Despite the potential of greater clinical benefit, ROP recurrences have been recorded many months following bevacizumab injection. 164 In contrast to laser therapy, where the recession is typically long-lasting and irreversible, the possibility of return following bevacizumab injection stresses the importance of periodic follow-up exams.

In the BEAT-ROP study, recurrences frequently occurred many months after the initial injection, with a mean onset of 16 weeks.[164]This places a special burden on the screening physician and the family to maintain frequent follow-up, frequently past 50 weeks of

gestation. Hu et al.'s early reports of recurrence identified children who had an initial response to bevacizumab treatment, but who then recurred aggressively and, in some cases, progressed to stage 4 or 5 detachments.[165]This highlighted the need for close follow-up, particularly for children who remained in zone I or posterior zone II despite being older. Some centers report much higher recurrence rates after ranibizumab, with some as high as 83% within six weeks of injection.[166-167]

Until ROP can be avoided, physicians who care for preterm newborns should use coordinated and timely measures to discover instances that require treatment. To implement local policies that help these newborns, neonatal intensivists, ophthalmic surgeons, coordinators of discharge, and ROP technicians must work together.

**NEWBORN SCREENING FOR RETINAL DISEASE**

Except for ROP, most pediatric retinal diseases are only discovered very late and are typically discovered by parents. A huge report by Abramson et al. showed that parents were the first to notice leukocoria in children with retinoblastoma 80% of the time, and the pediatrician was the first to notice it only 8% of the time.[168]This makes the case for using photoscreening to catch retinal diseases in children before they become symptomatic.

Li et al.'s large prospective study Digital fundus examinations of 3573 newborn children revealed that 0.6 percent had macular hemorrhages and 0.5% had retinal pathologies.[169]

Although the instrument used in this study—RetCam, Clarity MSI—was appropriate for use in a newborn nursery, it would be impractical to use it in an outpatient pediatric examination office. Several smartphone-based applications have recently been developed to assess

nonverbal children for amblyopia, cataracts, and retinal diseases.[170]Although these platforms are still in the early stages of evaluation, they have the potential to shorten the time it takes to diagnose retinal diseases, with the hope that earlier detection will reduce visual loss in this vulnerable population.

## LIMITATIONS OF TRADITIONAL CARE

Indirect ophthalmoscopy performed at the patient's side in NICU is a method of traditional retinopathy of prematurity screening. There are significant limitations, despite the fact that this had been successful in select infants with severe disease who require treatment. Ophthalmoscopic examinations are logistically challenging and necessitate considerable coordination and travel time. Sketches made by hand, which are subjective and qualitative, serve as documentation for the findings. [171,172,173]

Critical features like zone I and plus disease[174,175]may be misdiagnosed, posing a significant medical malpractice risk. As a result of these factors, fewer retinal specialists and pediatric ophthalmologists are willing to treat ROP. [176] Meanwhile, increased number of children are at risk for developing the disease. This is all due to the fact that there has been rising preterm birth and improved neonatal survival worldwide.

### A. TELEMEDICINE AS AN EMERGING APPROACH

Telemedicine is a new approach that has the ability to cut costs, improve care and raise quality. This might be especially important in places where healthcare is hard to get to. The trained staff in NICU, collect hospital records and images of the baby’s eye in this method. A remote ophthalmologist reviews the data and communicates management recommendations. Archiving retinal images has been of additional value in telemedicine.

In contrast to ophthalmoscopy with scleral depression, trained neonatal nurses may be able to capture high-quality retinal images causing less physiologic stress to infants.[177,178179]Newborn child photograph charts could be straightforwardly contrasted with reference images.Pictures give objective documentation of clinical discoveries, further develop acknowledgment of illness movement, improve correspondence, and make framework for schooling.[180]

**EVALUATION STUDIES**

Since the late 1990s, the predictive accuracy of telemedicine in ROP has been under evaluation. Essentially, all investigations used wide-point digital images captured by a newborn medical carer, ophthalmic surgeon or ophthalmic photographic artist. Despite differences in design and end measures, these studies evaluated telemedicine's diagnostic performance to a conventional dilated ophthalmoscopy standard. Schwartz and his colleagues investigated the efficacy of telemedicine in a group of kids at 30-32weeks PMA, they all had moderate/severe ROP. Telemedicine's sensitivity and specificity for identifying prethreshold or severe ROP had been 89% and 100% respectively.[181]From then on research had involved bigger and more extensive partners of sequentially enlisted babies.

Studies suggest that diagnosis of any ROP shows sensitivity of 46-97% and specificity of 49-100 percent while using reference standard of backhanded ophthalmoscopy.[177,182,183]For the most part, lower precision has been found while looking for mild ROP changes(e.g., stage 1) at newborn children of lower PMA. It is probably in light of the fact that younger infants have mild disease with signs which difficult to identify due to smaller eyeballs with decreased media visibility.[184]

Several researches have looked into the use of telemedicine to diagnose severe ROP. Ells and

his team members (371 tests from 36 newborn children) discovered that detecting "referral-warranted ROP" during sequential examinations of all newborns had a 100% sensitivity and a 96% specificity.[185] Wu and his colleagues (sequential testing on 43 newborn children) used telemedicine to diagnose pre-threshold or severe ROP and reported 100% sensitivity and 98% specificity.[186] Chiang and his coworkers. (163 tests from 64 newborn infants) exhibited sensitivity of 72-83percent and specificity of 90-99percent for detecting type 2 or worseROP, and sensitivity of 85-90percent and specificity of 95-97percent for detecting care reuired for ROP.[182] The multicenter prospective Photo-ROP trial found that sensitivity was 92percent and specificity was 37percent for detecting "clinically significant ROP" during weekly hospital examinations of the baby's medical clinic course.[187]

Chiang in his studies investigated the impact of post menstrual age and disease severity on telemedicine efficacy in a prospective research (248 tests from 67 newborn infants). At around 31 to 33weeks Post menstrual age, the sensitivity and specificity for detecting type 2 or worse ROP were 71-86percent and 93-97percent respectively, while the specificity for detecting treatment-requiring ROP was 94-100 percent. At 35-37weeks Post menstrual age, the sensitivity and specificity for identifying any ROP were 91-97percent and 98-100percent, respectively, for localization of type 2 or worse ROP, and 100 percent and 81-94percent, respectively, for discovery of therapy requiring ROP.[177] The precision is elevated in older newborn children which were in concurrence with past studies. [184]Dhaliwal et al. (245tests from 81 babies) directed a double-observer, masked, longitudinal prospective cohort study in which 2 pediatric ophthalmic surgeons were randomized to carry out assessments utilizing either telemedicine or ophthalmoscopy.

Outright arrangement among ophthalmoscopy and telemedicine was 96 percent for discovery

of stage 3, and 97 percent for recognition of plus disease.[188] Dai and his colleagues led a research in which a pediatric ophthalmologist screened all newborns via telemedicine imaging and ophthalmoscopy, pictures obtained were explored freely by a concealed grader. Images obtained by ophthalmoscopy were considered as a reference, sensitivity of telemedicine in identifying therapy requiring ROP (type 1 or worse) was 100percent and specificity was 98percent. 86 percent and 100 percent were the positive and negative predictive values respectively for identifying treatment-requiring ROP by telemedicine.[189]

Scott in his study compared telemedicine with ophthalmoscopy utilizing a plan in which the 2 techniques were performed by similar specialists in 67 successive newborn children. There was outright intragrader understanding of 86% (178/206 eyes) and kappa 0.66-0.85 among ophthalmoscopy and telemedicine. Among 14% (28/206 eyes) intra-expert errors, few babies were not detected by ophthalmoscopy such as mild ROP, this was detected by telemedicine. There were similar disparities including presence of zone I and plus disease, in which telemedicine gave hypothetical benefits by permitting analysts to survey their judgments or make more careful estimations of anatomic landmarks.[190]

The multicenter e-ROP study (5520 tests dissected from 1257 babies) carried out a framework in which pictures were caught via imaging technicians who deciphered along with trained nonphysician graders. The image grading of each eye was compared to indirect ophthalmoscopy image captured as a reference standard, in this study the sensitivity for detecting “referral-warranted ROP” was 82% and specificity was 90%. When both eyes of an infant were considered, the sensitivity was 90percent and specificity was 87percent.[191]

**Image Quality**

Ells in his studies discovered that 94% of sample images might be evaluated remotely, and 96% experiments successfully collected wide-angled photographs.[185] Wu and his colleagues discovered that 79% of the first retinal pictures and 78% of the subsequent retinal fundus images were approved.[187] According to the Photo-ROP cooperative organisation, 92percent of picture sets were accepted. Chiang in his studies found that telemedicine reported "unknown" diagnoses in 0-41% of tests at 31-33weeks PMA and 0-7percent of exams at 35-37 weeks PMA due to insufficient retinal coverage or poor picture quality.[177] Over a 6year timeframe, Lorenz et al showed that over 98% of 6460 telemedicine imaging examinations at 5 neonatal critical care units were appropriate. [192] Reduced picture quality may be related with pigmentation of funndus, hazy corneal and vitreous, narrower palpebral fissures, and mid dilating pupils.[177, 178, 186,193] Quinn et al concluded in a multicenter study that 91% of 5520 image sets taken by non-study-certified personnel had adequate quality, 6% had poor quality, and 3% were missing. [191]

**BARRIERS AND CHALLENGES**

Despite technological developments, medical licencing and a lack of standardised insurance coverage and reimbursement regulations have impeded broad adoption of telemedicine for ROP care. It is unknown what degree of diagnosis accuracy is necessary for the introduction of real-world ROP telemedicine systems because to worries regarding medicolegal responsibility.

Furthermore, due to the possibility of variation in reference for indirect ophthalmoscopy, it is challenging to rigorously evaluate accuracy. In the peripheral retinas of newborn, it may not always be possible to capture images of sufficient diagnostic quality, necessitating

reevaluation through sequential imaging. Lastly, implementing telemedicine in ROP necessitates physician acceptance and financial investments.

## Risk Factors

Preterm, LBW, a complicated stay at hospital, and increased exposure to supplemental $O_2$ are the most common factors of risk for ROP today.[48,94,194.195] During ROP epidemic of 1950s, it was abundantly documented that supplemental $O_2$ use for weeks without specific indication was a biggest reason for ROP development, but currently it is no longer the commonest cause of ROP since the middle of the 1970s. [48,94,194.195]

The rates of survival in extremely LBW children have improved as a result of recent advances in neonatal medicine. This group has a higher risk of developing ROP that necessitates management, with as many as 25% of children born at ≤750g developing the disease.[196]

The relevance of blood $CO_2$ levels in progression of ROP is controversial. In Beagles,Bauer and Widmayer[197] conducted a retrospective research on newborns with LBW in response to Flower's[198] observation that $CO_2$ exacerbated oxygen-induced retinal alterations. According to their findings, the most significant distinction between healthy infants and ROP-infected infants of equal gestation was made by higher arterial $CO_2$ values.[197,198]

Biglan[199]and Brown[194,200] along with their colleagues did not find a connection between the two, but they did find that children with "scarring retinopathy of prematurity" had reduced $CO_2$ levels in blood. Like ROP, this parameter and many others are likely to be linked to an unstable course of disease not in a causal way.

Numerous other newborn health concerns, including blue discoloration of mucous membranes, difficulty in breathing, mechanical ventilation, intraventricular bleeding, convulsions, transfusions, septicemia, inutero hypoxia, anaemia, PDA, and deficiency of vitamin E, have been linked to ROP..[51,195, 197-208] These associations necessitate additional investigation in order to identify causal relationships. Significant additional characteristics were discovered in CRYO-ROP study such as natural history cohort of 4099 babies born weighing <1251g were fairer complexion race, multiple deliveries, and being sent elsewhere for critical care.

**PRETERM DELIVERY**

Preterm baby is defined by WHO, a child birth that occurs prior to 37weeks. According to March of Dimes, there are 3 additional types of preterm delivery: extremely preterm (<28 weeks), very preterm (28-32 weeks), and late preterm (32-37 weeks). Birth weight was used prior to the modern methods of determining gestational age and was divided into three categories: extremely LBW (< 1,000 grams), very LBW (< 1,500 grams), and LBW (< 2,500 grams). Out of about140 million newborns born that year, an estimated 15 million were born prematurely or 10.6% of the global population. These rates vary by region, with Europe having lowest rate of 8.7% and North Africa having highest rate of 13.4%. Globally, the rate of preterm births has elevated from 9.8percent in 2000 to 10.6percent in 2014. The majority of preterm infants, or 84.7percent, are born moderately or late.[209]

According to Chawanpaiboon et al., it is estimated that 20.0% of preterm births are caused by multiple births.[210]According to Blencowe et al., there is a significant disparity in the survival rates of prematurely born babies between countries with high and low incomes. In high-income nations, more than 90% children born <28 weeks survive, whereas in low-income

nations, only 10% survive.[211]

According to Liu et al., in 2015, preterm birth complications accounted for 17.8% of all deaths in children under the five years.[212]Neonatal morbidities incorporate intraventricular drain (IVH), periventricular leukomalacia (PVL), bronchopulmonary dysplasia (BPD), necrotising enterocolitis (NEC), septicaemia, delayed growth and ROP. Cognitive impairment, reduced lung capacity, poor vascular health with hearing and visual disability are all long-term complications.[213]

The CRYO-ROP demonstrates the risk factors and consolidated it into a mathematical model that predicts threat of an unfavorable result for an eye that reaches severity of prethreshold ROP.[156]

**MATERNAL RISK FACTORS**

Maternal risk factors are being studied in the recent studies to link their correlation to development of ROP.

1. Hypertension in pregnancy

Although perinatal morbidities and hypertensive diseases in pregnancy are frequently linked[214,215]it is also known that these conditions are linked to greater levels of anti-angiogenic substances including placental growth factor and sFlt-1, an antagonist of vascular endothelial growth factor (VEGF).[214,216,217]By using univariate or multivariate analysis, a number of research discovered preeclampsia and eclampsia to be a major threat for ROP; nevertheless, various large studies discovered preeclampsia to be unrelated to ROP or to have a decreased risk of ROP.[214] A recent meta-analysis of 13 cohort studies found no conclusive link between ROP and hypertensive diseases of pregnancy.[214]

Various potential confounding factors, including prenatal medicine, related maternal diseases, and postnatal oxygen therapy, as well as varying research quality, may contribute to the results.

2. Gestational diabetes mellitus (GDM)

There are inconsistent findings about the relationship between maternal GDM and ROP, and diabetes has both a direct (e.g., elevated VEGF in retina secondary to elevated sugars) and indirect (e.g., link with RDS) influence on the development of ROP.[215,220] Infants of diabetic mothers had a greater prevalence of ROP, according to research conducted in the US between 1979 and 1981 as part of the National Collaborative Trial on Patent Ductus Arteriosus.[221]However, neither a Swedish study (1988-1990) of maternal risk factors for ROP nor an Israeli national database study (1995-2007) gave affirmation of the findings. A Turkish retrospective study recently detected maternal DM as an independent risk factor for both ROP and type I ROP in babies with birth weight 1.5kg.[214,222]

4. Maternal age

Miscarriage, genetic abnormalities, premature births, LBW, and 83,278 intrauterine development restrictions are some outcomes that have been linked to advanced maternal age.[214]The relationship between maternal age and Retinopathy of prematurity has been studied, and the findings are conflicting. Some studies show a rise in the risk with increasing maternal age,[223] while others show a reduction in proportion with increasing maternal age, one large Canadian cohort study found no correlation with maternal age.[224]The significant variations in maternal age ranges between researches might partially account for the contradictory findings.

5. Smoking

Tobacco has been found to upregulate VEGF in invitro experiments, and smoking while pregnant has been linked to LBW[214,225]Results regarding the link between maternal smoking and ROP are ambiguous.[214]A significant German study indicated that ROP development and growth limitation were both impacted by maternal smoking.[226]

The majority of these studies didn't look at smoking rates, which may be a crucial aspect to take into account in future research.

6. Maternal anemia

As per WHO standards, maternal anemia is considered anemia in pregnancy is defined as haemoglobin levels less than 11g/dl.[227]Anemic mothers tend to predispose increased premature deliveries.[2] ROP development was linked to maternal iron deficient anaemia, according to a Turkish study.[2] No such study has ever been conducted in India. ROP was substantially correlated with maternal blood leukocyte count, according to two investigations on maternal and neonatal variables.[228,229]

7. Delivery mode

Numerous studies have investigated the relationship between delivery method and ROP, with varying degrees of success. Some have shown a higher risk for ROP with vaginal birth, [230]some have found a higher risk with Caesarean section,[231]others have found no connections.[214]The gap may have been impacted by variances in prenatal medicines, reasons for delivery style and maternal conditions

8.Preterm Rupture of Membranes

On correlation between preterm premature rupture of membranes (PPROM) with ROP, contradicting findings have been published.[214]A Swedish study on the WINROP ("**Weight,**

**Insulin-like growth factor-1, Neonatal, ROP"**) an alarm discovered PPROM to have protective action against stage III ROP, contrary to findings from a Turkish study that PPROM >18 hours has been independently associated with elevated threat of type 1 ROP.[232,233]Varying outcome measures, a limited sample size, and other confounding factors that were taken into account in those studies could help to explain these contradictory results. A potential role for perinatal treatments (steroids) for PPROM in retinopathy of prematurity and the probability of a "prenatal phase" of ROP were suggested by 2 researches conducted in United States that found a lower proportion of worse ROP in PPROM groups compared to other causes of preterm birth.[234]

9. Chorioamnionitis

Numerous perinatal morbidities, such as cerebral palsy as well as bronchopulmonary dysplasia, have been linked to intrauterine inflammation, including chorioamnionitis, and numerous research point to a connection between chorioamnionitis and ROP.[235]Systemic inflammation hampered retinal angiogenesis in neonatal mice, according to animal research.[214,236] Chorioamnionitis was substantially related with ROP by univariate analyses, according to a meta-analysis of 27 papers published in 2014, although no connection was identified by multivariate analyses that corrected for GA. [237]

10. Twin / multiple births:

According to the CRYO-ROP research, singletons had a lower chance of developing ROP than multiplets. Multiple gestations were strongly related with ROP, according to further investigations [214]Multiple birth has been linked to ROP that requires treatment in a sequential order by Yang and coworkers,[238] whereas in a study by Port and his colleagues; a number of studies have found an increased proportion of Retinopathy of prematurity in singletons or

found no differences between singleton and multiple deliverys.[214, 239]This discrepancy may be brought on by different modes of delivery, other variable maternal factors and perinatal therapy, type of conception, and a failure to adjust for the risk factors, which is particularly crucial given that multiple gestations is linked to known risk factors of ROP like LBW.

11. Apgar score

Lower Apgar scores, which are generally considered to be a sign of poor newborn health, have been linked to greater occurrences of ROP. Lower Apgar scores were observed in infants with ROP in studies from China,[240] however, multivariate regression analysis revealed that the correlation between Apgar and Retinopathy of prematurity was not significant in the majority of these studies.

# MATERAIL & METHODS

# METHODS AND MATERIALS

**SOURCE OF DATA:**

A total of 80 preterm LBW babies of anemic mothers admitted in Neonatal Intensive Care Unit were enrolled in this Prospective Cross sectional Observational study visiting for ROP screening programme held at Neonatal Intensive Care Unit at R.L.J.H, Research Centre attached to Sri Devaraj Urs Medical College.

**STUDY DESIGN: Cross sectional observational study**

**STUDY PERIOD:1st January 2021 to 31st August 2022**

**INCLUSION CRITERIA:**

- All newborns born at 28-37 weeks of GA with birth weight < 2,500g of anaemic mothers admitted in intensive care unit of Sri Devaraj Urs Medical College
- Mothers having Hb levels less than 11g/dl and RBC count less than 4million cells/mcl in the 3rd trimester of pregnancy

**EXCLUSION CRITERIA:**

- Premature Babies lost to follow up.
- Premature babies who have completed 45 weeks of chronological age.

**Ethics approval and confidentiality: The institutional ethics review committee approved this study. The patient's identity and privacy were concealed, and confidentiality of data was ensured during the study.**

Informed consent :All patients fulfilling selection criteria were explained about the nature of

study. A written informed consent was taken from all participants prior to enrolment

**METHOD OF DATA COLLECTION**

a.Detailed general physical and ophthalmological examination of premature LBW infants of anaemic mothers were recorded followed by assessment of anaemic status of the mother in her 3rd trimester by collecting red blood cell count(RBC), haemoglobin levels, MCV, MCH and MCHC of mothers are recorded.

b.Retinopathy of prematurity was determined through fundus examination done by RETCAM and graded as per the "**International classification for retinopathy of prematurity (ICROP)**" specifying the locations (zone I-III) and severity of the disease (stage I-V) with or without plus disease and the extent of the disease.

- Zone 1: It is a circular zone focused on disc with radius twice distance from the disc to macular centre includes the posterior pole and it correlates an arc of about 60 degrees.
- Zone 2: It stretches from the periphery of zone I in a concentric circle tangential to the nasal ora serrata.
- Zone 3: It subtends to the remaining temporal crescent of retina anterior to zone II.

- Stage 1: Line of demarcation
- Stage 2: Ridge
- Stage 3: Ridge With Extra-retinal Fibro-vascular Proliferation
- Stage 4A: Extra-foveal RD
- Stage 4B: Partial RD Including the Fovea

- Stage 5: Total RD
- Florid form of ROP is a severe form of ROP, this is also called as Plus disease.

c. Anaemic status of the mother is obtained by collecting records of red blood cell count(RBC), haemoglobin levels, MCV, MCH and MCHC in her 3rd trimester. Based on the haemoglobin levels, the mothers were further divided into( as per the ICMR-1989)
   - Subgroup 1- mild anemia- 9-10.9g/dl
   - Subgroup 2- moderate anemia- 7-8.9g/dl
   - Subgroup 3- severe anemia-less than 7g/dl

**Procedure**: eyes of the newborn are dilated with the help of mydriatic drops (0.4% Tropicamide + 2.5% Phenylephrine) twice at 15minute interval and topical anaesthetic (proparacaine HCl 0.25%) is instilled before examining through a RETCAM. With the help of the lid speculum the eyes are opened and fundus photos are taken by RETCAM
at 4 weeks of chronological age.

**SAMPLE SIZE ESTIMATION**

Sample size was calculated based on previous studies prevalence of ROP being 73.6% with absolute precision of 10% and an estimated dropout rate of 10% and confidence level of 95%. The sample size is calculated by n'Master 2.0 which came to be around 75

ROP was considered as primary outcome variable. All data was coded and entered into excel sheet, all quantitative measures will be presented by mean and SD and qualitative or categorical data by frequency and percentage.

**STATISTICAL METHODS USED FOR THIS STUDY**

Difference in proportions will be compared by Chi Square (Bar- Fischer Exact Test).

Mean comparison between grades of anemia will be done by using t-test or Mann Whitney U test. p-value =/< 0.05 will be considered as statistically significant.

IBM SPSS version 22 was used for statistical analysis BDSS Corp., released 2020. coGuide Statistics software, Version 1.0, India: BDSS corp.

# RESULTS

# RESULTS

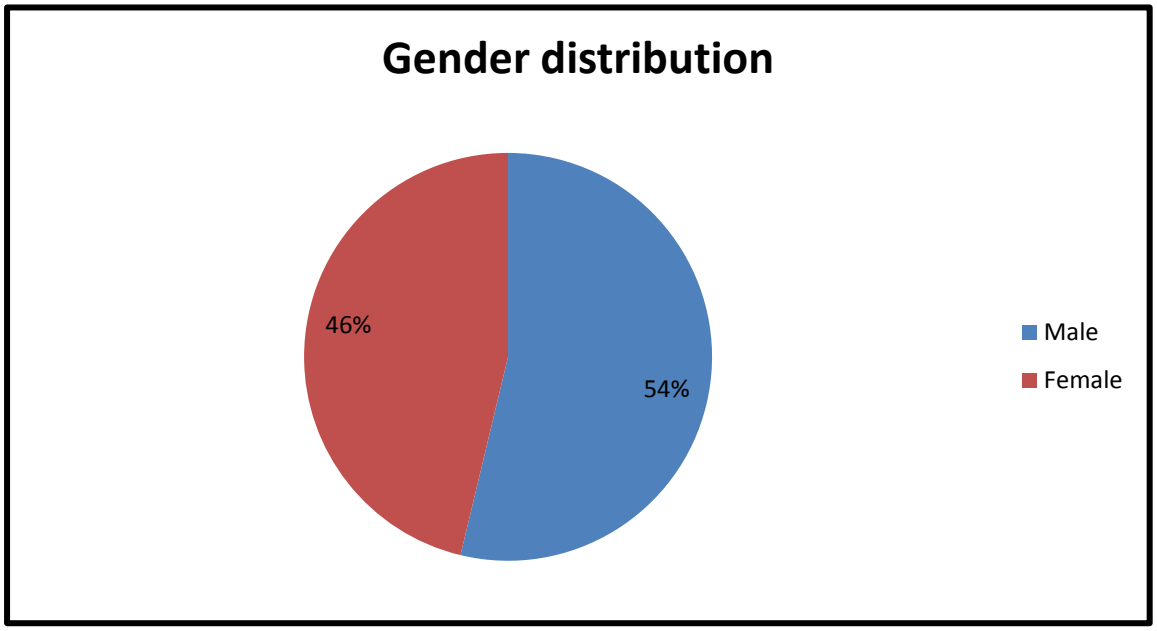
Out of 182 babies screened for presence of ROP, 80 babies fulfilled the inclusion criteria and were enrolled in the study. In included babies, 43 babies were seen to be males while other 37 babies were females.(graph 1) Out of the 182 babies 37 developed ROP shown in Table 3.

**Table 3: descriptive distribution of ROP preterm low birth babies in anemic and non-anemic mothers**

| DISEASES | ROP | NO ROP | TOTAL | Chi square value | P value |
|---|---|---|---|---|---|
| **MATERNAL ANEMIA** | 25 | 55 | 80 | 10.5101 | **0.001187** |
| **NO MATERNAL ANEMIA** | 12 | 90 | 102 | | |
| **Total** | 37 | 145 | 182 | | |

Table 4 depicts gender distribution in ROP. Graph 2 shows out of 80 babies 31.25% developed ROP with maternal anemia. It was seen that in these 25 preterm LBW babies also there was male preponderance. .

**GRAPH 1: Gender distribution in the study population (N=80)**

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**GRAPH 2: Proportion of ROP (N=80)**

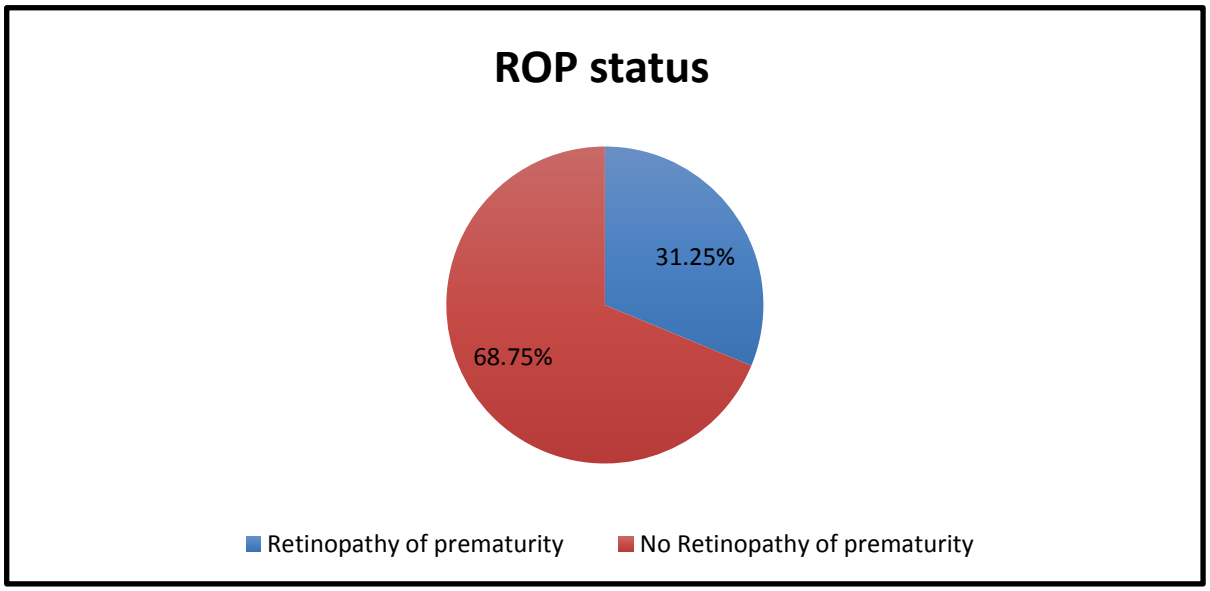
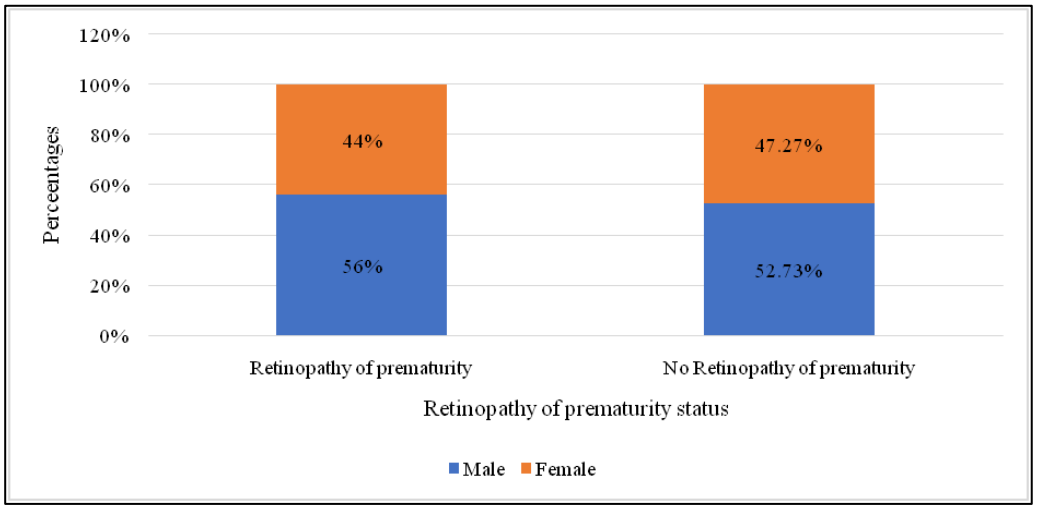


**Table 4: Comparison of ROP status with Gender distribution in study population**

| Gender | Retinopathy of prematurity status | | Chi square value | P value |
|---|---|---|---|---|
| | ROP (N=25) | No ROP (N=55) | | |
| Male | 14 (56.00%) | 29 (52.73%) | 0.07 | 0.7855 |
| Female | 11 (44.00%) | 26 (47.27%) | | |

**GRAPH 3: gender distribution in comparison with ROP status**



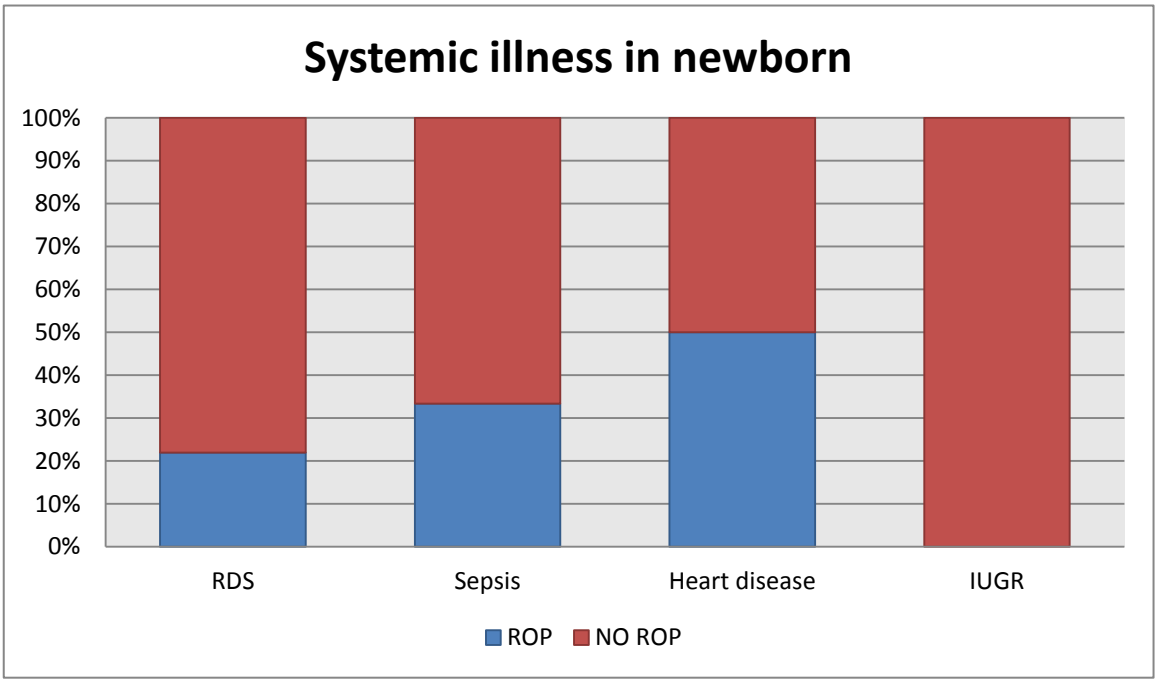

While assessing the proportion of ROP, in this study we also assessed neonatal and maternal risk factors which may also raise the proportion of development of ROP.

**Table 5: Comparison of ROP status with associated diseases in babies**

| Associated diseases | ROP status | |
|---|---|---|
| | **ROP (N=10)** | **No ROP (N=34)** |
| RDS | 7 (70.00%) | 25 (73.53%) |
| Sepsis | 2 (20.00%) | 4(11.76%) |
| Heart disease | 1 (10.00%) | 1 (2.94%) |
| IUGR | 0 (0.00%) | 4 (11.76%) |

While studying the proportion of ROP, we also studied other neonatal factors which may cause ROP. It was seen that out of 80 babies 44 developed other systemic disorders, Respiratory distress syndrome being most common out of all of them (72.72%). It was seen that 22.73% of ROP babies suffered from systemic illnesses. (table 5 and graph 4)

**Graph 4: Systemic illnesses of newborn**



In this study, mean birth weight was seen to be 1.58±0.41kg and weight at 4 weeks of chronological age was seen to be 1.60±0.49kg whereas ROP babies showed a median birth weight of 1.38kg and weight at 4 weeks was seen to be 1.40kg respectively. (table 6 and 7)

**Table 6: Clinical features of babies**

| S.NO | Name | Mean ± S.D | Median | Minimum | Maximum | 95% CI | |
|---|---|---|---|---|---|---|---|
| | | | | | | Lower CI | Upper CI |
| 1 | Chronological age (in weeks) | 4.00±0.00 | 4.00 | 4.00 | 4.00 | 4.00 | 4.00 |
| 2 | Birth weight | 1.58±0.41 | 1.53 | 0.92 | 3.40 | 1.49 | 1.67 |
| 3 | Present weight | 1.60±0.49 | 1.56 | 0.92 | 4.10 | 1.49 | 1.70 |
| 4 | APGAR (10mins) | 6.69±1.04 | 7.00 | 4.00 | 8.00 | 6.46 | 6.92 |

**Table 7: Comparison of ROP status with birth weight and current weight of babies**

| Parameter | Birth weight Median (IQR) | P Value | Present weight Median (IQR) | P Value |
|---|---|---|---|---|
| Retinopathy of prematurity (N=25) | 1.38(1.28 to 1.58) | 0.0041 | 1.40(1.2 to 1.6) | 0.0308 |
| No Retinopathy of prematurity (N=55) | 1.56(1.4 to 1.84) | | 1.60(1.38 to 1.79) | |

In this study, we have also discussed about the maternal risk factors that can cause ROP, it was seen that mean gestational age was 32.73±2.22weeks and mean maternal age was 24.50±3.77 years. (table 8 and 9)

Table 8: **Descriptive analysis of gestational age and maternal age in the study population**

| S.NO | Name | Mean ± S.D | Median | Minimum | Maximum | 95% CI | |
|---|---|---|---|---|---|---|---|
| | | | | | | Lower CI | Upper CI |
| 1 | Gestational age | 32.73±2.22 | 33.00 | 26.50 | 36.00 | 32.24 | 33.22 |
| 2 | Maternal age | 24.50±3.77 | 25.00 | 18.00 | 38.00 | 23.67 | 25.33 |

**Table 9: Comparison of ROP status with gestational age and maternal age**

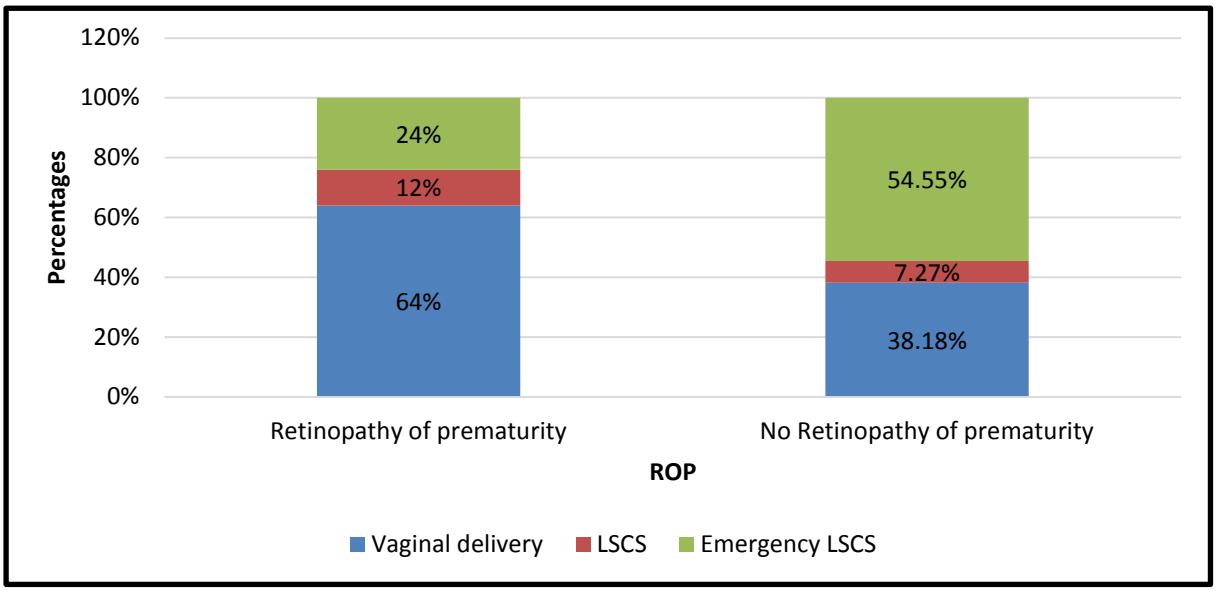
| Parameter | Gestational age Median (IQR) | P Value | Maternal age Median (IQR) | P Value |
|---|---|---|---|---|
| Retinopathy of prematurity (N=25) | 31.00(30.0 to 34.0) | <0.001 | 25.00(23.0 to 26.0) | 0.4314 |
| No Retinopathy of prematurity (N=55) | 33.00(32.0 to 35.0) | | 25.00(22.0 to 26.0) | |

We also compared the effect of mode of delivery in development of ROP, it was seen that majority of ROP babies were delivered by vaginal delivery( 64.00%). (table 10 and graph 5)

**Table 10: comparison between development of ROP with mode of delivery**

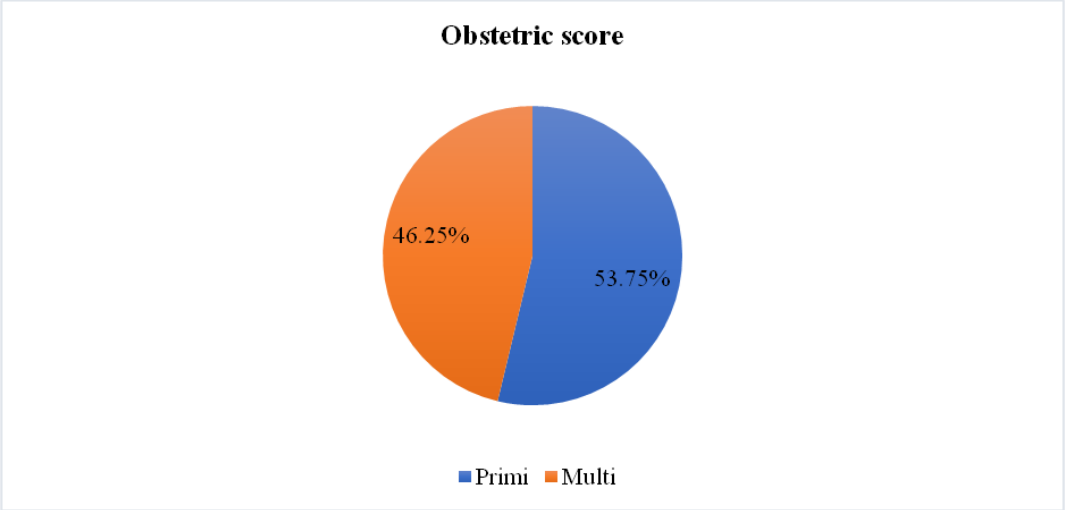
| Type of delivery | ROP status | | Chi square value | P value |
|---|---|---|---|---|
| | Retinopathy of prematurity (N=25) | No Retinopathy of prematurity (N=55) | | |
| Vaginal delivery | 16 (64.00%) | 21 (38.18%) | 6.48 | 0.0392 |
| Elective LSCS | 3 (12.00%) | 4 (7.27%) | | |
| Emergency LSCS | 6 (24.00%) | 30 (54.55%) | | |

**Graph 5: chart depicting different modes of delivery infants**




It was seen that in this study, primigravida were more predominant than multigravidas as shown in graph 6.

**Graph 6: chart on obstretic score in the study population (N=80)**




As shown in table 11 and 12, maternal blood parameters were computed and mean maternal Haemoglobin was 10.07±0.82g%, MCHC was 33.33±2.02g/dl, MCV was 79.14±5.89g/dl, MCH was 26.34±3.23picograms and RBC count was 3.49±0.24mil/$mm^3$. RBC count was statistically significant for the progression of ROP in premature LBW babies of anemic mothers

**Table 11: Descriptive analysis of maternal blood parameters**

| Name | Mean ± S.D | Median | Minimum | Maximum | 95% CI | |
|---|---|---|---|---|---|---|
| | | | | | Lower CI | Upper CI |
| **Haemoglobin %** | 10.07±0.82 | 10.40 | 7.00 | 10.90 | 9.89 | 10.25 |
| **Mean corpuscular haemoglobin concentration (g/dL)** | 33.33±2.02 | 33.00 | 28.00 | 42.10 | 32.88 | 33.77 |
| **Mean corpuscular volume (g/dL)** | 79.14±5.89 | 78.20 | 66.80 | 98.90 | 77.85 | 80.43 |
| **Mean corpuscular haemoglobin (picograms)** | 26.34±3.23 | 26.15 | 19.50 | 34.80 | 25.63 | 27.04 |
| **Red blood cells count (mil/mm3)** | 3.49±0.24 | 3.50 | 3.07 | 3.99 | 3.44 | 3.55 |

**Table 12: Comparison between development of ROP and maternal blood indices**

| Parameter | ROP | No ROP | P Value |
|---|---|---|---|
| **HB% Median (IQR)** | 10.40(9.9 to 10.7) | 10.40(9.3 to 10.65) | 0.3462 |
| **Mean corpuscular haemoglobin concentration Median (IQR)** | 33.20(32.4 to 34.4) | 32.90(31.9 to 34.65) | 0.2116 |
| **Mean corpuscular volume Median (IQR)** | 80.70(76.2 to 82.7) | 78.00(75.1 to 82.9) | 0.1353 |
| **Mean corpuscular haemoglobin Median (IQR)** | 26.20(24.5 to 28.5) | 25.70(24.15 to 28.5) | 0.1445 |
| **Red blood cells count (mil/mm3) Median (IQR)** | 3.62(3.5 to 3.8) | 3.46(3.26 to 3.6) | 0.0078 |

We also noticed that in this study, 24 babies with ROP, their mothers had mild anaemia during their 3rd trimester of pregnancy (table 11). It was seen that in these 24 babies, majority developed stage 2 ROP (68%) followed by AP-ROP (12%) and stage 1 ROP (16%). 1 baby born from a mother from moderate anemia developed stage 2 ROP with plus disease (table 13 and 14) (graph 7)

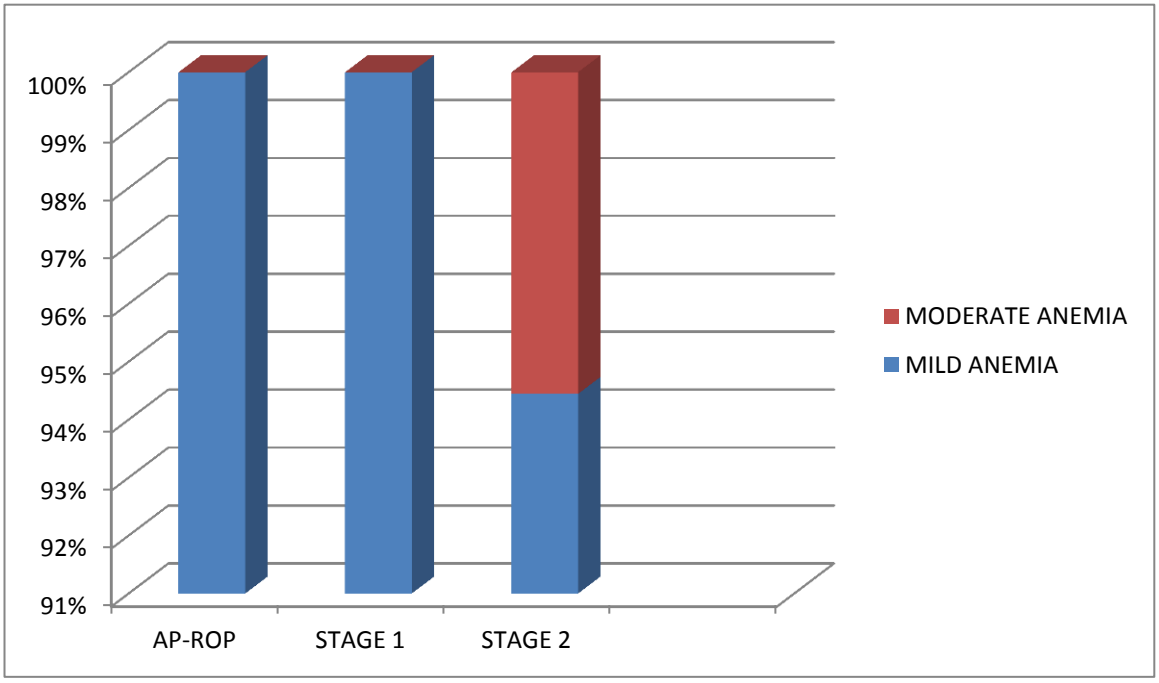
**Table 13: Proportion of ROP with severity of anemia**

| Maternal haemoglobin % | ROP(N=25) | |
|---|---|---|
| | Males | Females |
| MILD ANEMIA | 13 | 11 |
| MODERATE ANEMIA | 1 | 0 |
| SEVERE ANEMIA | 0 | 0 |

**Table 14: Severity of ROP**

| SEVERITY OF ROP | GRADING OF ANEMIA | | |
|---|---|---|---|
| | MILD | MODERATE | SEVERE |
| AP-ROP | 3(12%) | 0 | 0 |
| STAGE 1 | 4(16%) | 0 | 0 |
| STAGE 2 | 17(68%) | 1 | 0 |

**Graph 7: Severity of ROP**




19 ROP positive babies were subjected to indirect ophthalmoscope guided laser photocoagulation under topical anaesthesia. The other 6 were kept under observation for any development of ROP, no progression of ROP was seen in these caases. The cases were followed up until complete regression og new vessels was seen and vascularisation reached the equater.

# DISCUSSION

# DISCUSSION

ROP is preventable childhood blindness with multiple neonatal and maternal risk factors. In this study, we have screened 182 babies, out of which 80 babies fulfilled our inclusion criteria. A total of 37 ROP positive babies were diagnosed from these 182 babies, out of which 25 babies fulfilled our inclusion criteria suggesting that development of ROP is highly statistically significant in anemic mothers as shown in table 1. Similar finding was seen in a study conducted in Turkey.[2]

The proportion of development of ROP in premature LBW babies of anaemic mothers was seen to be 31.25% in this study, this is similar to previous studies conducted in India who stated that incidence of ROP is 20-59.9%.[9,10] out of these 25 babies 56% were males showing increased male preponderance. This male preponderance was seen even in previous studies suggesting that male gender is more at risk of development of ROP than females.[241, 242]

**Table 15: Descriptive analysis of different studies on ROP in India**

| **Author** | **Duration** | **Place** | **Percentage of ROP(%)** | **Percentage of ROP in anemic mother babies** |
|---|---|---|---|---|
| **Hungi, 2011**[243] | 1.5years | South India | 41.5 | NA |
| **Charan, 1995**[244] | 1year | North India | 47.3 | NA |
| **Ahuja, 2018**[245] | 1.5year | South India | 32.6 | NA |
| **Vasavada, 2018**[246] | 1.5year | Western India | 19.3 | NA |
| **Kumar, 2011**[247] | 5years | North India | 11.9 | NA |
| **Present study** | 1.5years | South India | 20.33 | 31.25% |

With respect to the maternal blood parameters, we compared the maternal haemoglobin, MCHC, MCH, MCV and RBC with development of ROP in premature LBW infants and observed that statistical significance was present only with RBC count, suggesting that RBC count is a sensitive indicator for development of ROP in premature LBW infants of anaemic mothers.

While studying for the proportion of ROP, we also studied the other risk factors that may predispose to development of ROP. It was seen that in neonatal factors such as LBW and weight at 4weeks chronological age of the baby is statistically significant values for determining the risk of development of ROP in premature babies. This finding was similar to some studies. [48,94,194.195,196]

Some studies suggest that systemic neonatal diseases can increase the incidence of development of ROP[5], in this study it was seen that 40% of the 25 ROP babies had pre-existing neonatal diseases like Respiratory distress syndrome (70%), sepsis (20%), heart disease (10%). No babies with growth retardation were seen to develop ROP. C. Le et al also found that RDS was the most prevalent disease to cause ROP in premature babies.[248]

We also collected data on systemic maternal diseases and found out that 64% of the ROP positive babies had other maternal and neonatal systemic diseases along with maternal anemia suggesting that maternal anemia increases the incidence of other maternal diseases and neonatal diseases which increase the proportion of ROP. In recent studies, a correlation is attempted to be made between development of ROP and maternal diseases, such as maternal anemia, gestational diabetes, smoking etc.[2,222,225,249]

With respect to the maternal risk factors for development of ROP as shown in several studies, early gestational age of neonate and vaginal mode of delivery had elevated risk of development of ROP and was found statistically significant in development of ROP in preterm LBW infants.[250] The median gestational age of ROP babies in this study was seen to be 31weeks which correlated with other studies.[251] Mean gestational age of neonates in anaemic mother babies was found to be 31.7weeks

We also noticed that majority of ROP positive premature babies mothers suffered from mild anemia and no change in severity is seen in ROP is seen with increase in severity of ROP.

Limitations of the study are small sample size and short duration of study; further studies are required with a larger sample size.

Strength of this study is that till date no study has been conducted in India to determine the relation between development of ROP and anemic mothers. This study also determines the proportion of ROP being 31.25% which is similar to that of the proportion of ROP developing in the nation suggesting anemia in mothers is also one of the major cause of development of this disease.

# CONCLUSION

# CONCLUSION

Hence in our study we conclude that in order to reduce the development of ROP, measure should not be taken after the birth of the baby but during pregnancy itself, as development of the retinal vessels starts in the intrauterine period and is completed 1 month after birth. Neonatal as well as maternal factors both are responsible for proper development of the retina.

# SUMMARY

# SUMMARY

Retinopathy of prematurity earlier named as retrolental fibroplasia is a vasoproliferative retinal disease affecting preterm babies. It is considered as the 3rd epidemic disease of the world with majority of cases originating from middle income countries. It is one of the common avoidable cause of blindness worldwide.

This is a prospective cross-sectional study conducted from January 1, 2021 to August 31, 2022 in NICU of RL Jalappa Hospital attached to Sri Devaraj Urs Medical College, Tamaka, Kolar.a total of 182 baies were screened for presence of ROP out of this 80 infants were included in this study as per the inclusion and exclusion criteria. It was seen that the development of ROP in preterm LBW newborns of anemic mothers is statistically significant (p=0.0011) and its proportion is 31.25%.

64% of these ROP babies had other neonatal and maternal systemic illnesses that aided in the development of ROP. 36% were seen to develop ROP with maternal anemia as an independent risk factor. Majority of the babies in this study were born to mothers with mild anemia which showed a varied severity of development of ROP in infants. RBC count was seen to be statistically significant for the development of anemia. Birth weight (p=0.0041), gestational age (p=<0.001), vaginal delivery (p=0.0392) were statistically significant factors for development of ROP in this study.

Hence, this study concluded by stating the proportion of development of ROP in LBW preterm infants of anemic mothers is 31.25%. Thereby, care should be taken during pregnancy itself to avoid the development of ROP.

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# BIBLIOGRAPHY


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# ANNEXURES

# ANNEXURE-I

## STUDY PROFORMA

**CASE NO.-** **OP NO.-**

**NAME –**

**AGE-OCCUPATION**

**ADDRESS-**

**BABY DETAILS**

**SEX-**

**GESTATIONAL AGE-** **CHRONOLOGICAL AGE-**

**BIRTH WEIGHT-** **PRESENT WEIGHT-**

**APGAR SCORE-** **DOB-**

**RISKS--NEONATAL JAUNDICE/ SEPSIS/RDS/T1DM/THYROID DISORDER**

**MATERNAL DETAILS:**

**AGE-**

**HABITS-**

**PAST HISTORY**

**TYPE OF DELIVERY-**

**OBSTRETIC HISTORY**

**Obstretic score:**

**LMP-** **EDD-**

**PARA-** **ABORTION-**

**INVESTIGATIONS OF 3$^{RD}$ TRIMESTER OF PREGANCY**

**HB%**

**MCH-** **MCHC-**

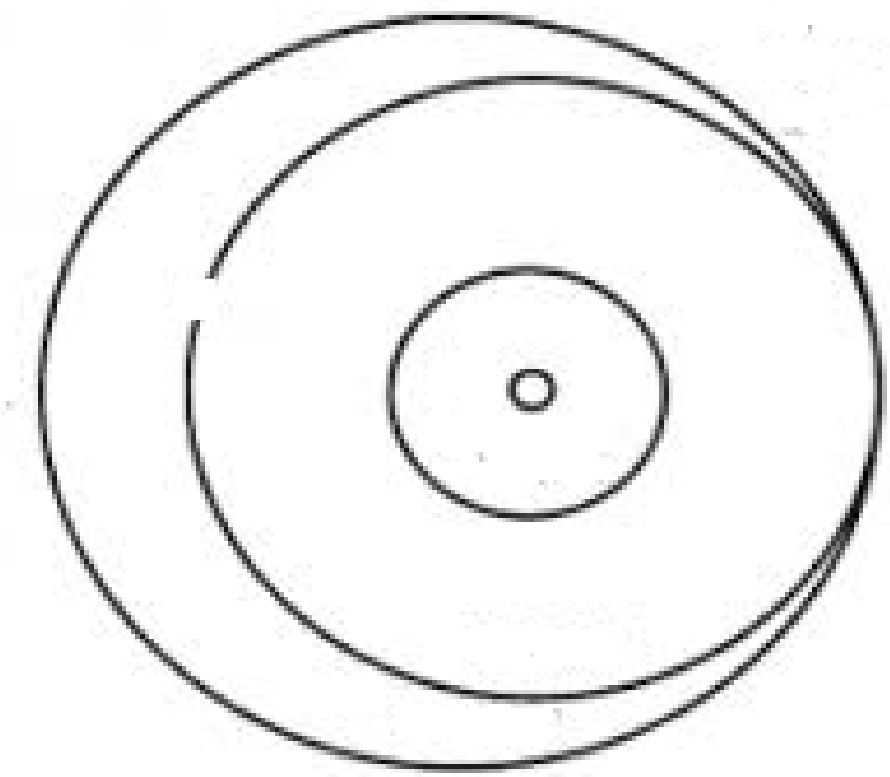
**MCV-** **RBC COUNT-**

**OCULAR EXAMINATION OF THE BABY**

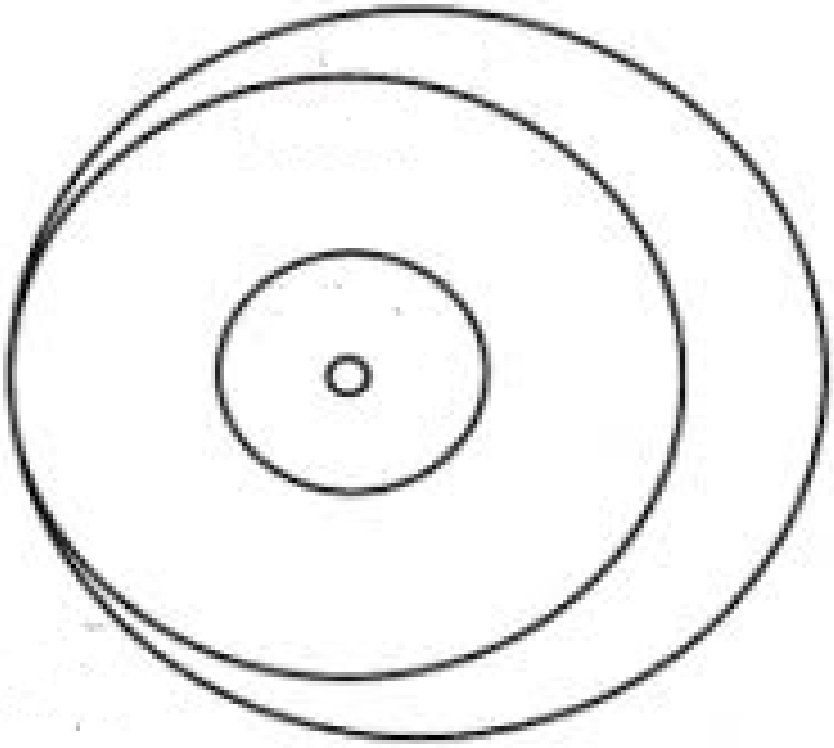
| S.N0. | ANTERI0R SEGMENT | RIGHT EYE | LEFT EYE |
|---|---|---|---|
| 1 | LIDS AND ADNEXA | | |
| 2 | CONJUNCTIVA | | |
| 3. | CORNEA | | |
| 4. | IRIS PATTERN | | |
| 5 | PUPIL | | |
| 6 | LENS | | |

**FUNDUS EXAMINATION**

RIGHT EYE



LEFT **EYE**



## DIAGNOSIS

## ADVICE

**ANNEXURE II**

**SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR - 563101.**

**INFORMED CONSENT FORM**

**Case no:**

**IP no:**

**TITLE: TO DETERMINE THE PROPORTION OF ROP IN PREMATURE, LOW BIRTH WEIGHT INFANTS OF ANEMIC MOTHERS**

I _____ mother of the baby have been explained in detail, in a language that I can comprehend that retinopathy of prematurity is a disease of retinal vasculature affecting the premature babies. ROP if left undetected/untreated will lead to visual impairement/ even blindness.

RETCAM will help in taking pictures of baby's fundus enabling us to know the status of the retinal vasculature which in turn will help us pick any abnormality if present at the earliest by regular follow ups

I, the undersigned, agree to participate in this study and authorize the collection and disclosure of personal information and examination of my baby's fundus outlined in this consent form.

I understand the purpose of this study, the risks and benefits of the ROP screening proceduresuch as temporary decrease in heart rate and temporary cessation of breathing that may occur in my baby and the confidential nature of the information that will be collected and disclosed during the study. The information collected will be used only for research.

I have had the opportunity to ask questions regarding the various aspects of this study and my questions have been answered to my satisfaction.

I understand that I remain free to withdraw the participation from this study at any time and this will not change the future care.

Participation in this study does not involve any extra cost to me.

| Name | Signature | Date | Time |
|---|---|---|---|
| Mother of the baby: | | | |
| Witness: | | | |
| Primary Investigator/ Doctor: | | | |

**<u>ಶ್ರೀ ದೇವರಾಜ್ ಯುಆರ್ಎಸ್ ಉನ್ನತ ಶಿಕ್ಷಣ ಮತ್ತು ಸಂಶೋಧನೆ ಅಕಾಡೆಮಿ, ತಮಕ, ಕೋಲಾರ - 563101.</u>**

ಮಾಹಿತಿ ನೀಡಿದ ಒಪ್ಪಿಗೆ ನಮೂನೆ

ಪ್ರಕರಣ ಸಂಖ್ಯೆ:

IP ಸಂಖ್ಯೆ:

ಶೀರ್ಷಿಕೆ:

ರಕ್ತಹೀನತೆ ಹೊಂದಿರುವ ತಾಯಂದಿರ ಅಕಾಲಿಕ, ಕಡಿಮೆ ಜನನ ತೂಕದ ಶಿಶುಗಳಲ್ಲಿ ರಾಪ್ನ ಪ್ರಮಾಣವನ್ನು ನಿರ್ಧರಿಸಲು

ನಾನು _____ ಮಗುವಿನ ತಾಯಿಯನ್ನು ವಿವರವಾಗಿ ವಿವರಿಸಲಾಗಿದೆ, ಪ್ರಿಮೆಚ್ಯೂರಿಟಿಯ ರೆಟಿನೋಪತಿ ಅಕಾಲಿಕ ಶಿಶುಗಳ ಮೇಲೆ ಪರಿಣಾಮ ಬೀರುವ ರೆಟಿನಾದ ನಾಳೀಯ ಕಾಯಿಲೆಯಾಗಿದೆ ಎಂದು ನಾನು ಗ್ರಹಿಸಬಹುದಾದ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಲಾಗಿದೆ. ROP ಅನ್ನು ಪತ್ತೆಹಚ್ಚದಿದ್ದರೆ/ಚಿಕಿತ್ಸೆ ಮಾಡದೆ ಬಿಟ್ಟರೆ ದೃಷ್ಟಿದೋಷ/ಕುರುಡುತನಕ್ಕೂ ಕಾರಣವಾಗುತ್ತದೆ.

ರೆಟಿಕಾಮ್ ಮಗುವಿನ ಫಂಡಸ್ನ ಚಿತ್ರಗಳನ್ನು ತೆಗೆಯಲು ಸಹಾಯ ಮಾಡುತ್ತದೆ, ಇದು ರೆಟಿನಾದ ನಾಳಗಳ ಸ್ಥಿತಿಯನ್ನು ತಿಳಿದುಕೊಳ್ಳಲು ಅನುವು ಮಾಡಿಕೊಡುತ್ತದೆ, ಇದು ನಿಯಮಿತವಾದ ಫಾಲೋ ಅಪ್ಗಳ ಮೂಲಕ ಯಾವುದೇ ಅಸಹಜತೆಯನ್ನು ಹೊಂದಿದ್ದರೆ ಅದನ್ನು ಆಯ್ಕೆ ಮಾಡಲು ನಮಗೆ ಸಹಾಯ ಮಾಡುತ್ತದೆ.

ನಾನು, ಕೆಳಗೆ ಸಹಿ ಮಾಡಿದ್ದೇನೆ, ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಸಮ್ಮತಿಸುತ್ತೇನೆ ಮತ್ತು ವೈಯಕ್ತಿಕ ಮಾಹಿತಿಯ ಸಂಗ್ರಹಣೆ ಮತ್ತು ಬಹಿರಂಗಪಡಿಸುವಿಕೆ ಮತ್ತು ಈ ಒಪ್ಪಿಗೆಯ ನಮೂನೆಯಲ್ಲಿ ವಿವರಿಸಿರುವ ನನ್ನ

ಮಗುವಿನ ನಿಧಿಯ ಪರೀಕ್ಷೆಯನ್ನು ಅಧಿಕೃತಗೊಳಿಸುತ್ತೇನೆ.

ಈ ಅಧ್ಯಯನದ ಉದ್ದೇಶ, ROP ಸ್ಕ್ರೀನಿಂಗ್ ಕಾರ್ಯವಿಧಾನದ ಅಪಾಯಗಳು ಮತ್ತು ಪ್ರಯೋಜನಗಳು ಅಂದರೆ ಹೃದಯ ಬಡಿತದಲ್ಲಿ ತಾತ್ಕಾಲಿಕ ಇಳಿಕೆ ಮತ್ತು ನನ್ನ ಮಗುವಿನಲ್ಲಿ ಸಂಭವಿಸಬಹುದಾದ ಉಸಿರಾಟದ ತಾತ್ಕಾಲಿಕ ನಿಲುಗಡೆ ಮತ್ತು ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಸಂಗ್ರಹಿಸಿದ ಮತ್ತು ಬಹಿರಂಗಪಡಿಸುವ ಮಾಹಿತಿಯ ಗೌಪ್ಯ ಸ್ವರೂಪವನ್ನು ನಾನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ. . ಸಂಗ್ರಹಿಸಿದ ಮಾಹಿತಿಯನ್ನು ಸಂಶೋಧನೆಗೆ ಮಾತ್ರ ಬಳಸಲಾಗುತ್ತದೆ.

ಈ ಅಧ್ಯಯನದ ವಿವಿಧ ಅಂಶಗಳ ಬಗ್ಗೆ ಪ್ರಶ್ನೆಗಳನ್ನು ಕೇಳಲು ನನಗೆ ಅವಕಾಶವಿದೆ ಮತ್ತು ನನ್ನ ಪ್ರಶ್ನೆಗಳಿಗೆ ನನ್ನ ತೃಪ್ತಿಗೆ ಉತ್ತರಿಸಲಾಗಿದೆ.

ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಈ ಅಧ್ಯಯನದಿಂದ ಭಾಗವಹಿಸುವಿಕೆಯನ್ನು ಹಿಂಪಡೆಯಲು ನಾನು ಮುಕ್ತನಾಗಿರುತ್ತೇನೆ ಮತ್ತು ಇದು ಭವಿಷ್ಯದ ಕಾಳಜಿಯನ್ನು ಬದಲಾಯಿಸುವುದಿಲ್ಲ ಎಂದು ನಾನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ.

ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವಿಕೆಯು ನನಗೆ ಯಾವುದೇ ಹೆಚ್ಚುವರಿ ವೆಚ್ಚವನ್ನು ಒಳಗೊಂಡಿರುವುದಿಲ್ಲ.

| ಹೆಸರು | ಸಹಿ | ದಿನಾಂಕ | ಸಮಯ |
|---|---|---|---|
| ಮಗುವಿನ ತಾಯಿ: | | | |
| ಸಾಕ್ಷಿ: | | | |
| ಪ್ರಾಥಮಿಕ ತನಿಖಾಧಿಕಾರಿ/ವೈದ್ಯ: | | | |

**ANNEXURE III**

**SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR - 563101.**

## PATIENT INFORMATION SHEET

This information is to help you understand the purpose of the study "TO DETERMINE THE PROPORTION OF ROP IN PREMATURE, LOW BIRTH WEIGHT INFANTS WITH ANEMIC MOTHERS". You are invited to take part voluntarily in this research study, it is important that you read and understand the purpose, procedure, benefits and discomforts of the study.

1. What is the purpose of this study?

   To determine the proportion of rop in premature, low birth weight infants with anemic mothers

2. What are the various investigations being used? Are there any associated risks?

   Blood investigation reports of mothers done in 3rd trimester are collected and analysed for presence of anemia. ROP screening procedure is done under aseptic precautions and after the consent of the parents for the screening procedure.

   There may be temporary decrease in heart rate and temporary cessation of breathing during the ROP screening procedure, for which appropriate care by the NICU support staff will be taken and if required the procedure will be stopped

3. What is the benefit for me as a participant?

   Participation in this research study may not change the final outcome of your eye condition. However, patients in the future may benefit as a result of knowledge gained from this study. You will not be charged extra for any of the procedures performed during the research study. Your taking part in this study is entirely voluntary. You may refuse to take

part in the study or you may stop your participation in the study at any time, without a penalty or loss of any benefits to which you were otherwise entitled before taking part in this study.

**CONFIDENTIALITY**

Your medical information will be kept confidential by the study doctor and staff and will not be made publicly available. Your original records may be reviewed by your doctor or ethics review board. For further information/ clarification please contact Dr B.O. HANUMANTHAPPA, SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR - 563101.Contact no: 9844177487 and 7892540646 to DR. PANAAH SHETTY

**ಶ್ರೀ ದೇವರಾಜ್ ಯುಆರ್ಎಸ್ ಉನ್ನತ ಶಿಕ್ಷಣ ಮತ್ತು ಸಂಶೋಧನೆ ಅಕಾಡೆಮಿ, ತಮಕ, ಕೋಲಾರ - 563101.**

## ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆ

ಈ ಮಾಹಿತಿಯು ನಿಮಗೆ ಅಧ್ಯಯನದ ಉದ್ದೇಶವನ್ನು ಅರ್ಥಮಾಡಿಕೊಳ್ಳಲು ಸಹಾಯ ಮಾಡುವುದು "ಅಕಾಲಿಕ, ಕಡಿಮೆ ಜನನ ತೂಕದ ಶಿಶುಗಳಲ್ಲಿ ರಕ್ತಹೀನತೆಯ ತಾಯಂದಿರಲ್ಲಿ ರಾಪ್ ಪ್ರಮಾಣವನ್ನು ನಿರ್ಧರಿಸಲು". ಈ ಸಂಶೋಧನಾ ಅಧ್ಯಯನದಲ್ಲಿ ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಪಾಲ್ಗೊಳ್ಳಲು ನಿಮ್ಮನ್ನು ಆಹ್ವಾನಿಸಲಾಗಿದೆ, ಅಧ್ಯಯನದ ಉದ್ದೇಶ, ಕಾರ್ಯವಿಧಾನ, ಪ್ರಯೋಜನಗಳು ಮತ್ತು ಅನಾನುಕೂಲಗಳನ್ನು ನೀವು ಓದುವುದು ಮತ್ತು ಅರ್ಥಮಾಡಿಕೊಳ್ಳುವುದು ಮುಖ್ಯವಾಗಿದೆ.

1. ಈ ಅಧ್ಯಯನದ ಉದ್ದೇಶವೇನು?

ರಕ್ತಹೀನತೆಯ ತಾಯಂದಿರೊಂದಿಗೆ ಅಕಾಲಿಕ, ಕಡಿಮೆ ತೂಕದ ಶಿಶುಗಳಲ್ಲಿ ರಾಪ್ನ ಪ್ರಮಾಣವನ್ನು ನಿರ್ಧರಿಸಲು

2. ಯಾವ ವಿವಿಧ ತನಿಖೆಗಳನ್ನು ಬಳಸಲಾಗುತ್ತಿದೆ? ಯಾವುದೇ ಸಂಬಂಧಿತ ಅಪಾಯಗಳಿವೆಯೇ?

3 ನೇ ತ್ರೈಮಾಸಿಕದಲ್ಲಿ ಮಾಡಿದ ತಾಯಂದಿರ ರಕ್ತದ ತನಿಖಾ ವರದಿಗಳನ್ನು ರಕ್ತಹೀನತೆಯ ಉಪಸ್ಥಿತಿಗಾಗಿ ಸಂಗ್ರಹಿಸಲಾಗುತ್ತದೆ ಮತ್ತು ವಿಶ್ಲೇಷಿಸಲಾಗುತ್ತದೆ. ROP ಸ್ಕ್ರೀನಿಂಗ್ ವಿಧಾನವನ್ನು ಅಸೆಪ್ಟಿಕ್ ಮುನ್ನೆಚ್ಚರಿಕೆಗಳ ಅಡಿಯಲ್ಲಿ ಮತ್ತು ಸ್ಕ್ರೀನಿಂಗ್ ಕಾರ್ಯವಿಧಾನಕ್ಕಾಗಿ ಪೋಷಕರ ಒಪ್ಪಿಗೆಯ ನಂತರ ಮಾಡಲಾಗುತ್ತದೆ.

ROP ಸ್ಕ್ರೀನಿಂಗ್ ಪ್ರಕ್ರಿಯೆಯಲ್ಲಿ ಹೃದಯ ಬಡಿತದಲ್ಲಿ ತಾತ್ಕಾಲಿಕ ಇಳಿಕೆ ಮತ್ತು ಉಸಿರಾಟದ ತಾತ್ಕಾಲಿಕ ನಿಲುಗಡೆ ಇರಬಹುದು, ಇದಕ್ಕಾಗಿ NICU ಬೆಂಬಲ ಸಿಬ್ಬಂದಿಯಿಂದ ಸೂಕ್ತ ಕಾಳಜಿಯನ್ನು

ತೆಗೆದುಕೊಳ್ಳಲಾಗುತ್ತದೆ ಮತ್ತು ಅಗತ್ಯವಿದ್ದರೆ ಕಾರ್ಯವಿಧಾನವನ್ನು ನಿಲ್ಲಿಸಲಾಗುತ್ತದೆ.

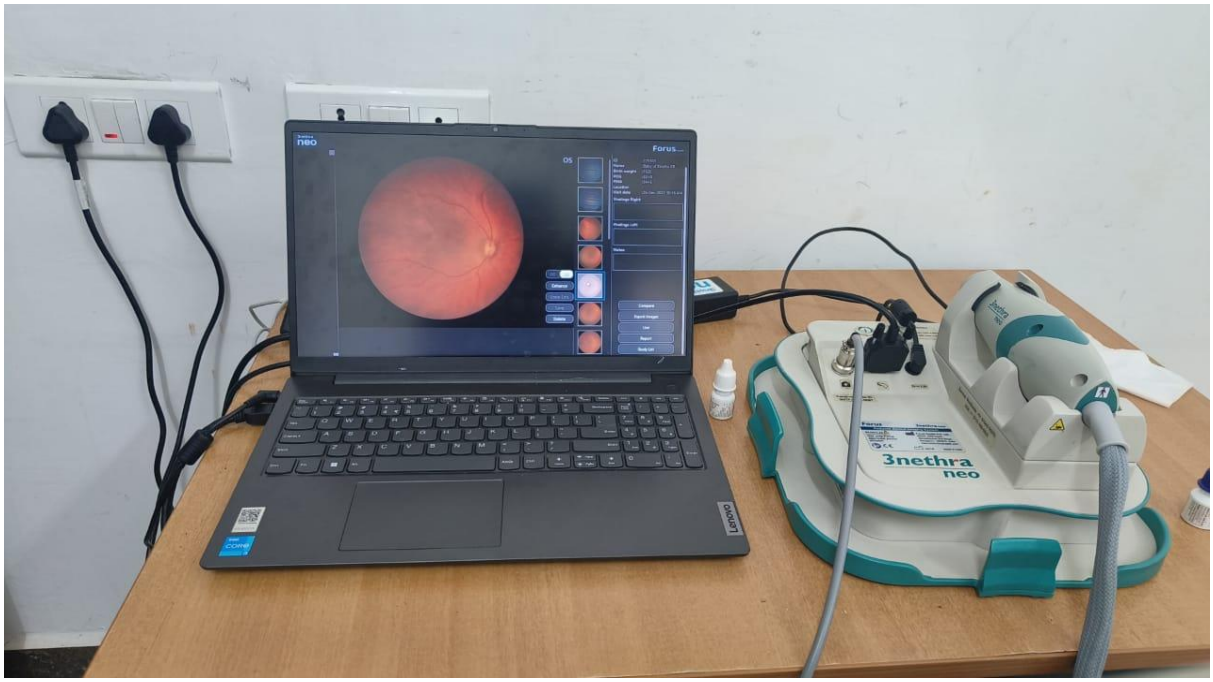
3. ಭಾಗವಹಿಸುವವನಾಗಿ ನನಗೆ ಏನು ಪ್ರಯೋಜನ?

ಈ ಸಂಶೋಧನಾ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವಿಕೆಯು ನಿಮ್ಮ ಕಣ್ಣಿನ ಸ್ಥಿತಿಯ ಅಂತಿಮ ಫಲಿತಾಂಶವನ್ನು ಬದಲಾಯಿಸದಿರಬಹುದು. ಆದಾಗ್ಯೂ, ಈ ಅಧ್ಯಯನದಿಂದ ಪಡೆದ ಜ್ಞಾನದ ಪರಿಣಾಮವಾಗಿ ಭವಿಷ್ಯದಲ್ಲಿ ರೋಗಿಗಳು ಪ್ರಯೋಜನ ಪಡೆಯಬಹುದು. ಸಂಶೋಧನಾ ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ನಡೆಸಿದ ಯಾವುದೇ ಕಾರ್ಯವಿಧಾನಗಳಿಗೆ ನಿಮಗೆ ಹೆಚ್ಚುವರಿ ಶುಲ್ಕ ವಿಧಿಸಲಾಗುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನೀವು ಭಾಗವಹಿಸುವುದು ಸಂಪೂರ್ಣವಾಗಿ ಸ್ವಯಂಪ್ರೇರಿತವಾಗಿದೆ. ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ನಿರಾಕರಿಸಬಹುದು ಅಥವಾ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವ ಮೊದಲು ನೀವು ಅರ್ಹರಾಗಿದ್ದ ಯಾವುದೇ ಪ್ರಯೋಜನಗಳ ದಂಡ ಅಥವಾ ನಷ್ಟವಿಲ್ಲದೆಯೇ ನೀವು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವುದನ್ನು ನಿಲ್ಲಿಸಬಹುದು.

ಗೌಪ್ಯತೆ

ನಿಮ್ಮ ವೈದ್ಯಕೀಯ ಮಾಹಿತಿಯನ್ನು ಅಧ್ಯಯನ ವೈದ್ಯರು ಮತ್ತು ಸಿಬ್ಬಂದಿ ಗೌಪ್ಯವಾಗಿಡುತ್ತಾರೆ ಮತ್ತು ಸಾರ್ವಜನಿಕವಾಗಿ ಲಭ್ಯವಾಗುವಂತೆ ಮಾಡಲಾಗುವುದಿಲ್ಲ. ನಿಮ್ಮ ಮೂಲ ದಾಖಲೆಗಳನ್ನು ನಿಮ್ಮ ವೈದ್ಯರು ಅಥವಾ ಎಥಿಕ್ಸ್ ರಿವ್ಯೂ ಬೋರ್ಡ್ ಪರಿಶೀಲಿಸಬಹುದು. ಹೆಚ್ಚಿನ ಮಾಹಿತಿಗಾಗಿ / ಸ್ಪಷ್ಟೀಕರಣಕ್ಕಾಗಿ ದಯವಿಟ್ಟು ಡಾ ಬಿ.ಓ. ಹನುಮಂತಪ್ಪ, ಶ್ರೀ ದೇವರಾಜ್ ಯುಆರ್ಎಸ್ ಉನ್ನತ ಶಿಕ್ಷಣ ಮತ್ತು ಸಂಶೋಧನಾ ಅಕಾಡೆಮಿ, ತಮಕ, ಕೋಲಾರ - 563101.ಸಂಪರ್ಕ ಸಂಖ್ಯೆ: 9844177487 ಮತ್ತು 7892540646 ಗೆ ಡಾ. ಪಣ ಶೆಟ್ಟಿ

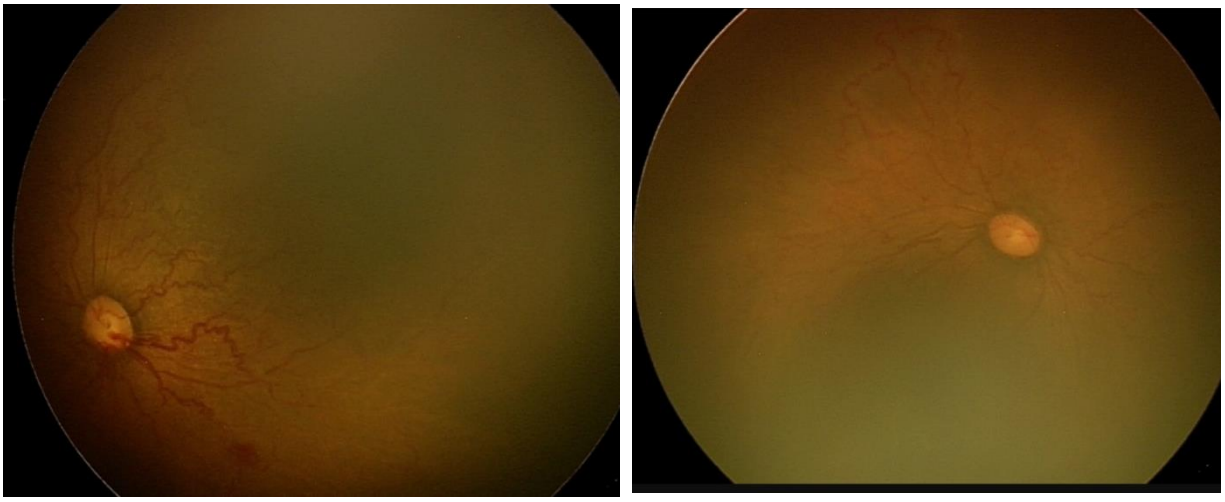
# ANNEXURE IV



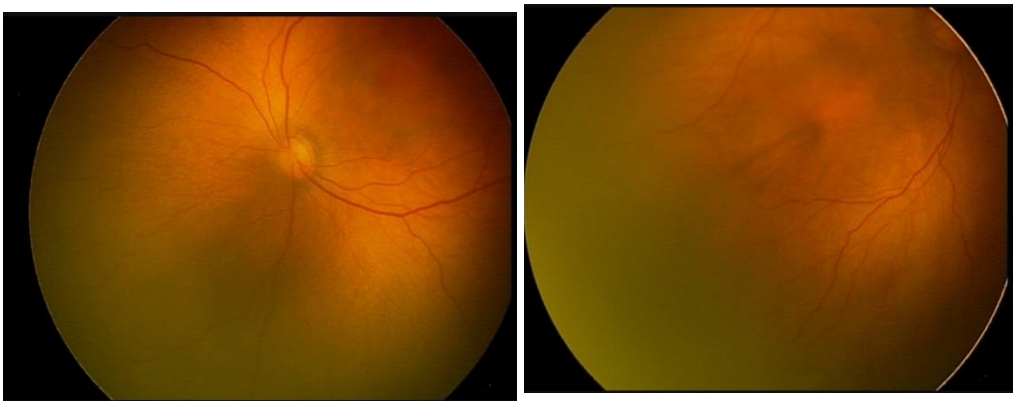

**Photograph 1: laptop connected to RETCAM**

A B

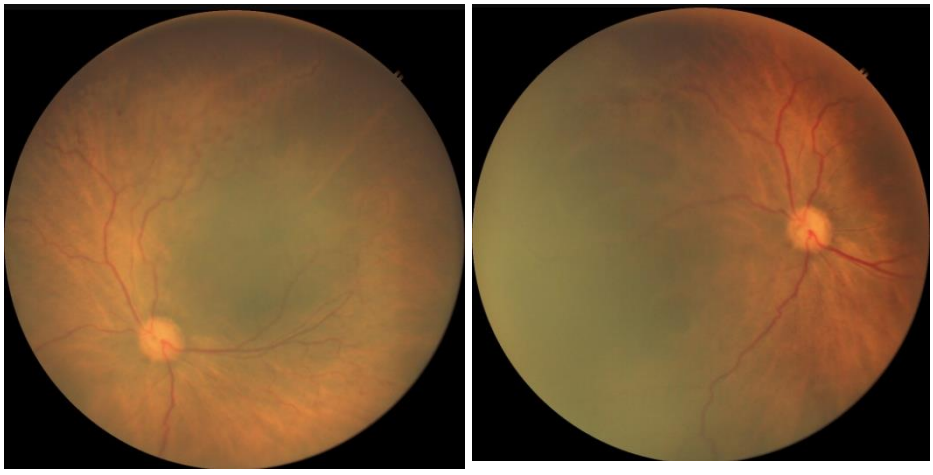
**Photograph 2: (a)and (b) depict Examination of fundus by RETCAM**



**Photograph 3: BE:Aggressive Proliferative ROP**



**Photograph 4: Stage 2 ROP in zone 2**



**Photograph 5: Stage 1 in zone 1**

# MASTER CHART

# KEY TO MASTER CHART

**RDS**: respiratory distress syndrome

**Wks**: weeks

**LSCS**: lower segment Caesarian section

**ROP**: retinopathy of prematurity

**APROP:** aggressive proliferativr ROP

**P**: Para

**L:** living

**A:** abortion

**Hb:** haemoglobin

**MCHC:** mean corpuscular hemoglobin concentration

**MCV:** mean corpuscular volume

**MCH:** mean corpuscular hemoglobin

**RBC:** red blood cell

| S NO | UHID NO. | gender | date of birth | gestational age | chronological age | birth weight | present weight (kg) | APGAR | associated diseases | maternal age | mothers uhid | past history | type of delivery | LMP | EDD | OBSTRETIC SCORE | HBg% | MCHC | MCV | MCH | RBC count(mil/mm3) | ROP status | TREATMENT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 892169 | MALE | 27/01/2021 | 31wks+ 5 days | 4weeks | 1.4kg | 1.34 | *6/10 | RDS | 25 | 892146 | PREECAMPSIA | vaginal delivery | NA | 24/02/2020 | P2L2A1 | 10.8 | 32 | 76.2 | 24 | 3.28 | NO ROP | |
| 2 | 892992 | male | 01/02/2021 | 33wks | 4weeks | 1.56kg | 1.42 | *6/10 | SEPSIS | 26 | 892854 | * | VAGINAL DELIVERY | NA | 01/03/2020 | PRIMI GRAVIDA | 10.3 | 36 | 86 | 21.1 | 3.07 | NO ROP | |
| 3 | 234795 | FEMALE | 23/06/2020 | 32wks | 4weeks | 1.4kg | 4.1 | *6/10 | * | 24 | 89563 | * | vaginal delivery | 05/11/2020 | 12/08/2020 | PRIMIGRAVIDA | 10.2 | 42.1 | 80 | 34.8 | 3.64 | NO ROP | |
| 4 | 871619 | MALE | 13/10/2020 | 35wks+ 3 days | 4weeks | 1.48kg | 1.48 | *6/10 | RDS | 26 | 859656 | eclampsia | emergency LSCS | 27/01/2020 | 04/11/2020 | P1L1 | 9.6 | 29.9 | 78 | 27.6 | 3.5 | NO ROP | |
| 5 | 899347 | MALE | 08/07/2020 | 31wks+5days | 4weeks | 1.66kg | 1.66 | *6/10 | SEPSIS | 24 | 896044 | * | EMRGENCY LSCS | NA | 13/08/2020 | P1L1 | 10.3 | 32.9 | 78.2 | 25.7 | 3.3 | NO ROP | |
| 6 | 896589 | FEMALE | 16/02/2021 | 30wks | 4WEEKS | 1.83kg | 1.8 | *7/10 | HEART DISEASE | 28 | 896571 | * | VAGINAL DELIVERY | NA | 20/04/2021 | P4L2D2 | 9 | 34.4 | 80.7 | 27.7 | 3.27 | NO ROP | |
| 7 | 888367 | MALE | 08/01/2021 | 33wks | 4weeks | 1.54kg | 1.46 | *6/10 | * | 33 | 888166 | TWIN PREGNANCY | LSCS | 22/05/2020 | 28/02/2021 | P3L3 | 8.1 | 31 | 69 | 21 | 3.46 | NO ROP | |
| 8 | 904654 | MALE | 19/03/2021 | 32wks | 4weeks | 1.41kg | 1.3 | *7/10 | RDS | 21 | 904326 | * | VAGINAL DELIVERY | NA | 19/04/2021 | P1L1 | 10.4 | 36 | 86 | 31 | 3.79 | OD:APROP+ VASCULARIZATION TILL ZONE 1 ANT CLOSE TO DISC, OS WHITE RELEX | BE LASER PHOTOCOAGULATION |
| 9 | 904758 | MALE | 23/03/2021 | 31wks+2 days | 4weeks | 1.3kg | 1.26 | *7/10 | * | 25 | 904595 | PREECLAMSIA | VAGINAL DELIVERY | 15/08/2020 | 22/05/2021 | P2L2 | 9.6 | 34.1 | 83.5 | 28.5 | 3.62 | STAGE 1 ROP IN ZONE 2 | |
| 10 | 910266 | MALE | 25/03/2021 | 31wks | 4weeks | 1.6kg | 1.56 | *5/10 | probable sepsis | 24 | 906388 | TWIN PREGNANCY | VAGINAL DELIVERY | NA | 25/04/2021 | P1L2 | 10.7 | 31.9 | 82.3 | 26.2 | 3.62 | STAGE 2 ROP IN ZONE 2 | |
| 11 | 906049 | FEMALE | 25/03/2021 | 31wks | 4weeks | 1.58kg | 1.6 | *5/10 | SEPSIS | 24 | 906388 | TWIN PREGNANCY | VAGINAL DELIVERY | NA | 25/04/2021 | P1L2 | 10.7 | 31.9 | 82.3 | 26.2 | 3.62 | STAGE 2 ROP IN ZONE 2 WITH EARLY PLUS | LASER PHOTOCOAGULATION |
| 12 | 907407 | MALE | 13/04/2021 | 31wks | 4WEEKS | 1.46kg | 1.48 | *7/10 | * | 26 | 909387 | IMMINENT ECLAMPSIA | emergency LSCS | 07/09/2020 | 14/06/2021 | P2L2A1 | 10.9 | 31.9 | 82.3 | 26.2 | 3.24 | NO ROP | |
| 13 | 910267 | MALE | 04/04/2021 | 33weeks | 4weeks | 1.82kg | 1.7 | *5/10 | RDS | 25 | 907528 | * | EMERGENCY LSCS | NA | 28/04/2021 | PRIMIGRAVIDA | 8.8 | 31 | 69 | 21 | 3.17 | NO ROP | |
| 14 | 907012 | FEMALE | 01/04/2021 | 31wks | 4weeks | 1.11kg | 0.92 | *6/10 | * | 24 | 906850 | TWIN PREGNANCY | VAGINAL DELIVERY | not known | 01/05/2021 | PRIMIGRAVIDA | 9 | 31.1 | 75.1 | 23.3 | 3.53 | NO ROP | |
| 15 | 907013 | FEMALE | 01/04/2021 | 31wks | 4weeks | 1.38kg | 1.2 | *7/10 | * | 24 | 906850 | TWIN PREGNANCY | VAGINAL DELIVERY | not known | 01/05/2021 | PRIMIGRAVIDA | 9 | 31.1 | 75.1 | 23.3 | 3.53 | STAGE 2 ROP IN ZONE 2 WITH EARLY PLUS | LASER PHOTOCOAGULATION |
| 16 | 912132 | FEMALE | 07/04/2021 | 31wks | 4weeks | 1.38kg | 1.14 | *5/10 | RDS | 25 | 906333, **908191** | TWIN PREGNANCY | VAGINAL DELIVERY | 25/08/2020 | 04/06/2021 | **PRIMIGRAVIDA** | 10.7 | 36 | 86 | 31 | 3.25 | STAGE 2 ROP IN ZONE 2 WITH PLUS DISEASE | LASER PHOTOCOAGULATION |
| 17 | 911900 | FEMALE | 07/04/2021 | 31wks | 4weeks | 1.08kg | 1.3 | *7/10 | * | 25 | 908191 | TWIN PREGNANCY | VAGINAL DELIVERY | 25/08/2020 | 04/06/2021 | PRIMIGRAVIDA | 10.7 | 36 | 86 | 31 | 3.25 | NO ROP | |
| 18 | 911663 | MALE | 22/04/2021 | 30wks | 4WEEKS | 1.28kg | 1.14 | *6/10 | * | 26 | 911615 | TWIN PREGNANCY | LSCS | 21/09/2020 | 28/06/2021 | P2L3 | 10.6 | 32.6 | 80.1 | 26.1 | 352 | STAGE 2 IN ZONE 2 WITH EARLY PLUS DISEASE | LASER PHOTOCOAGULATION |
| 19 | 911664 | MALE | 22/04/2021 | 30wks | 4weeks | 1.4kg | 1.4 | *6/10 | * | 26 | 911615 | TWIN PREGNANCY | LSCS | 21/09/2020 | 28/06/2021 | P2L3 | 10.65 | 32.6 | 80.1 | 26.1 | 3.52 | STAGE 1 IN ZONE 2 with plus disease | LASER PHOTOCOAGULATION |
| 20 | 916181 | MALE | 03/05/2021 | 35Wks | 4weeks | 1.55kg | 1.94 | *7/10 | RDS | 18 | 914164 | PRE ECLAMPSIA | VAGINAL DELIVERY | 29/08/2020 | 05/06/2021 | PRIMIGRAVIDA | 10.8 | 35 | 78 | 27 | 3.53 | NO ROP | |
| 21 | 914600 | FEMALE | 04/05/2021 | 32wks | 4weeks | 1.78kg | 1.712 | *7/10 | * | 24 | 914585 | * | emergency LSCS | 12/08/2020 | 19/05/2021 | P2L2 | 8.3 | 31 | 69 | 21 | 3.11 | NO ROP | |
| 22 | 254100 | FEMALE | 24/05/2021 | 35wks | 4weeks | 1.68kg | 1.6 | *7/10 | * | 26 | 919907 | breech presentation | emergency LSCS | 17/09/2020 | 24/06/2021 | PRIMIGRAVIDA | 10.4 | 33 | 76 | 25 | 3.6 | NO ROP | |
| 23 | 253389 | FEMALE | 17/05/2021 | 35wks | 4weeks | 2.62kg | 2.96 | *7/10 | * | 20 | 920827 | * | VAGINAL DELIVERY | NA | 01/06/2021 | PRIMIGRAVIDA | 9.2 | 28.4 | 71.1 | 20.2 | 3.56 | NO ROP | |
| 24 | 942616 | MALE | 11/08/2021 | 31WKS | 4weeks | 1.3kg | 1.24 | *7/10 | * | 21 | 930908 | * | emergency LSCS | 01/01/2021 | 08/10/2021 | PRIMIGRAVIDA | 10 | 36 | 87 | 31 | 3.83 | APROP+ VASCULARIZATION TILL ZONE 1 ANT CLOSE TO DISC | |
| 25 | 936471 | MALE | 02/08/2021 | 26WKS+ 4DAYS | 4weeks | 1.22kg | 1.04 | *8/10 | RDS | 25 | 936443 | * | VAGINAL DELIVERY | 28/01/2021 | 04/11/2021 | PRIMIGRAVIDA | 9.2 | 35 | 84 | 30 | 3.12 | STAGE 2 ROP IN ZONE 2 WITH PLUS DISEASE | |
| 26 | 938969 | FEMALE | 12/08/2021 | 3OWKS+4DAYS | 4weeks | 1.8KG | 1.48 | *6/10 | * | 27 | 938952 | * | VAGINAL DELIVERY | 10/07/2021 | 17/10/2021 | P2L2A1 | 10.5 | 32 | 70 | 23 | 3.5 | STAGE 1 ROP WITH PLUS DISEASE | LASER PHOTOCOAGULATION |
| 27 | 938216 | FEMALE | 10/08/2021 | 31WKS+3DAYS | 4weeks | 1.07kg | 1.07 | *4/10 | * | 21 | 938200 | eclampsia | VAGINAL DELIVERY | 01/01/2021 | 08/10/2021 | P3L2D1 | 10.3 | 35 | 78 | 27 | 3.92 | APROP+ VASCULARIZATION TILL ZONE 1 ANT CLOSE TO DISC | LASER PHOTOCOAGULATION |
| 28 | 943010 | FEMALE | 30/08/2021 | 34WEEKS | 4weeks | 1.38 | 1.74 | *7/10 | * | 25 | 924944 | breech presentation | emergency LSCS | 02/01/2021 | 09/10/2021 | P2L1A1 | 10.6 | 32.4 | 75.5 | 24.5 | 3.83 | NO ROP | |
| 29 | 943257 | MALE | 31/08/2021 | 35 WEEKS | 4WEEKS | 1.86 | 1.94 | *7/10 | RDS | 22 | 943244 | PREECLAMPSIA | emergency LSCS | 17/12/2021 | 23/09/2021 | P1A3 | 10.6 | 35 | 78 | 27 | 3.31 | NO ROP | |
| 30 | 943258 | MALE | 31/08/2021 | 35 WEEKS | 4weeks | 1.08 | 1.2 | *7/10 | RDS | 22 | 943244 | PRE ECLAMPSIA | emergency LSCS | 17/12/2021 | 23/09/2021 | P1A3 | 10.6 | 35 | 78 | 27 | 3.31 | NO ROP | |
| 31 | 940859 | FEMALE | 21/08/2021 | 33WEEKKS | 4weeks | 1.66 | 1.5 | *7/10 | RDS | 25 | 940855 | ABRUPTIO PLACENTA | emergency LSCS | 30/12/2020 | 07/10/2021 | P2L1 | 10 | 36 | 87 | 31 | 3.23 | NO ROP | |
| 32 | 941715 | MALE | 25/08/2021 | 34WEEKS | 4weeks | 1.64KG | 1.4 | *7/10 | RDS | 26 | 941713 | * | VAGINAL DELIVERY | 27/12/2020 | 04/10/2021 | PRIMIGRAVIDA | 8.2 | 31.5 | 66.8 | 21.1 | 3.89 | NO ROP | |
| 33 | 938721 | MALE | 11/08/2021 | 32WEEKS | 4weeks | 1.6 | 2 | *7/10 | RDS | 32 | 938201 | PRE ECLAMPSIA | emergency LSCS | 24/12/2020 | 30/09/2021 | P1L1A1 | 10 | 32.6 | 80.1 | 26.1 | 3.28 | STAGE 2 ROP IN ZONE 2 WTH PLUS DISEASE | LASER PHOTOCOAGULATION |
| 34 | 939248 | MALE | 03/08/2021 | 34 WEEKS | 4weeks | 1.58 | 1.98 | *7/10 | * | 23 | 935789 | * | VAGINAL DELIVERY | 29/11/2020 | 05/09/2021 | P1L1 | 8.5 | 34 | 71 | 24 | 3.5 | STAGE 2 ROP IN ZONE 2 | LASER PHOTOCOAGULATION |
| 35 | 940909 | FEMALE | 21/08/2021 | 35WEEKS | 4WEEKS | 2 | 1.74 | *8/10 | RDS | 20 | 940858 | TWIN PREGNANCY, ECLAMPSIA | LSCS | 17/12/2020 | 23/09/2021 | PRIMGRAVIDA | 10.5 | 36 | 86 | 31 | 3.38 | NO ROP | |
| 36 | 940990 | FEMALE | 22/08/2021 | 35WEEKS | 4weeks | 2.14 | 1.8 | *8/10 | RDS | 20 | 940858 | TWIN PREGNANCY, ECLAMPSIA | LSCS | 17/12/2020 | 23/09/2021 | PRIMGRAVIDA | 10.5 | 36 | 86 | 31 | 3.38 | NO ROP | |
| 37 | 950316 | FEMALE | 30/09/2021 | 32WEEKS | 4weeks | 1.54 | 1.44 | *8/10 | RDS | 26 | 922580 | * | emergency LSCS | 24/10/2020 | 31/07/2021 | P2L2 | 10.8 | 32.4 | 75.5 | 24.5 | 3.8 | NO ROP | |
| 38 | 78966 | MALE | 30/09/2021 | 35 WEEKS | 4weeks | 1.56 | 1.7 | *8/10 | * | 28 | 944925 | ANTEPARTUM HEMORRHAGE, PRECLAMPSIA | | 26/01/2021 | 02/11/2021 | PRIMIGRAVIDA | 7 | 31 | 69 | 21 | 3.3 | NO ROP | |
| 39 | 949944 | MALE | 28/09/2021 | 35weeks | 4weeks | 1.38 | 1.32 | *8/10 | * | 28 | 948026 | TWIN PREGNANCY, PREECLAMPSIA | VAGINAL DELIVERY | 19/01/2021 | 26/10/2021 | P3L4 | 10.4 | 33 | 76 | 25 | 3.5 | NO ROP | |
| 40 | 949945 | MALE | 28/09/2021 | 35weeks | 4weeks | 1.38 | 1.74 | *8/10 | SEPSIS | 28 | 948026 | TWIN PREGNANCY, PREECLAMPSIA | VAGINAL DELIVERY | 19/01/2021 | 26/10/2021 | P3L5 | 10.4 | 33 | 76 | 25 | 3.5 | NO ROP | |
| 41 | 23562 | FEMALE | 29/09/2021 | 35weeks | 4WEEKS | 1.84 | 1.77 | *8/10 | RDS | 25 | 950033 | TWIN PREGNANCY | EMERGENCY LSCS | 25/01/2021 | 01/11/2021 | P2L3 | 10.1 | 34 | 74 | 25 | 3.5 | NO ROP | |
| 42 | 85696 | MALE | 29/09/2021 | 35weeks | 4weeks | 1.88 | 1.9 | *8/10 | IUGR | 25 | 950033 | TWIN PREGNANCY | EMERGENCY LSCS | 25/01/2021 | 01/11/2021 | P2L3 | 10.1 | 34 | 74 | 25 | 3.5 | NO ROP | |
| 43 | 45866 | FEMALE | 30/09/2021 | 32 WEEKS | 4weeks | 1.59 | 1.7 | *6/10 | * | 24 | 949770 | PREECLAMPSIA | VAGINAL DELIVERY | 16/02/2021 | 23/11/2021 | PRIMIGRAVIDA | 10.6 | 36 | 85 | 30 | 3.5 | NO ROP | |
| 44 | 95623 | MALE | 21/09/2021 | 35 WEEKS | 4weeks | 1.33 | 1.26 | *6/10 | RDS | 18 | 947887 | * | VAGINAL DELIVERY | 15/01/2021 | 22/10/2021 | PRIMIGRAVIDA | 10.7 | 34 | 82 | 28 | 3.6 | NO ROP | |
| 45 | 66891 | FEMALE | 11/03/2022 | 32WEEKS | 4weeks | 1.72 | 1.48 | *6/10 | RDS | 28 | 66881 | * | EMERGENCY LSCS | 18/07/2021 | 24/04/2022 | PRIMIGRAVIDA | 10.8 | 31.9 | 82.3 | 26.2 | 3.12 | NO ROP | |
| 46 | 66892 | FEMALE | 11/03/2022 | 32WEEKS | 4weeks | 1.4 | 1.36 | *6/10 | RDS | 28 | 66881 | * | EMERGENCY LSCS | 18/07/2021 | 24/04/2022 | PRIMIGRAVIDA | 10.8 | 31.9 | 82.3 | 26.2 | 3.12 | NO ROP | |
| 47 | 60680 | FEMALE | 29.01.22 | 34 WEEKS | 4WEEKS | 1.12 | 1.64 | *6/10 | RDS | 26 | 60668 | ECLAMPSIA | VAGINAL DELIVERY | 19/05/2021 | 23/02/2022 | PRIMIGRAVIDA | 8.6 | 33.5 | 86.8 | 29.1 | 3.85 | NO ROP | |
| 48 | 107962 | FEMALE | 28/01/2022 | 34 WEEKS | 4weeks | 1.8 | 1.9 | *6/10 | * | 19 | 61917 | ANTEPARTUM HEMORRHAGE | EMERGENCY LSCS | 21/06/2021 | 14/03/2022 | G2A1 | 10.5 | 32.4 | 75.5 | 24.5 | 3.8 | STAGE 2 ROP IN ZONE 2 IN PLUS DISEASE | |
| 49 | 73813 | MALE | 15.03.22 | 33WEEKS | 4weeks | 1.06 | 1.1 | *6/10 | * | 23 | 69199 | TWIN PREGNANCY | EMERGENCY LSCS | 27/07/2021 | 04/05/2022 | PRIMIGRAVIDA | 10.6 | 31.5 | 71.4 | 22.5 | 3.72 | NO ROP | |
| 50 | 73806 | MALE | 25.03.22 | 33WEEKS | 4weeks | 1.58 | 1.66 | *6/10 | * | 23 | 69199 | TWIN PREGNANCY | EMERGENCY LSCS | 27/07/2021 | 04/05/2022 | PRIMIGRAVIDA | 10.6 | 31.5 | 71.4 | 22.5 | 3.72 | NO ROP | |
| 51 | 70077 | MALE | 30.03.22 | 33WEEKS | 4weeks | 1.52 | 1.46 | *6/10 | * | 24 | 40946 | ANTEPARTUM ECLAMPSIA | VAGINAL DELIVERY | 26/07/2021 | 02/05/2022 | PRIMIGRAVIDA | 10.9 | 34.9 | 82.2 | 28.7 | 3.99 | NO ROP | |

| S NO | UHID NO. | gender | date of birth | gestational age | chronological age | birth weight | present weight (kg) | APGAR | associated diseases | maternal age | mothers uhid | past history | type of delivery | LMP | EDD | OBSTRETIC SCORE | HBg% | MCHC | MCV | MCH | RBC count(mil/mm3) | ROP status | TREATMENT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 52 | 70507 | MALE | 25.03.22 | 35 WEEKS | 4weeks | 1.68 | 1.66 | *6/10 | * | 21 | 70428 | PREECLAMPSIA, HEART DISEASE | EMERGENCY LSCS | 07/07/2021 | 13/04/2022 | PRIMIGRAVIDA | 9 | 34.1 | 83.5 | 28.5 | 3.16 | NO ROP | |
| 53 | 51384 | MALE | 25.03.22 | 35 WEEKS | 4WEEKS | 1.98 | 1.86 | *7/10 | probable sepsis | 21 | 70428 | PREECLAMPSIA, HEART DISEASE | EMERGENCY LSCS | 07/07/2021 | 13/04/2022 | PRIMIGRAVIDA | 9 | 34.1 | 83.5 | 28.5 | 3.16 | NO ROP | |
| 54 | 73814 | FEMALE | 9.03.22 | 30WEEKS | 4weeks | 1.36 | 1.26 | *7/10 | RDS | 25 | 67705 | PPROM | EMERGENCY LSCS | NA | NA | PRIMIGRAVIDA | 9.9 | 31.5 | 70.7 | 22.3 | 3.44 | NO ROP | |
| 55 | 45632 | MALE | 16/02/2022 | 35 WEEKS | 4weeks | 1.5 | 1.6 | *7/10 | * | 24 | 61171 | PPROM | EMERGENCY LSCS | 18/06/2021 | 25/03/2022 | PRIMIGRAVIDA | 10.7 | 32.9 | 78.2 | 25.7 | 3.51 | NO ROP | |
| 56 | 143108 | FEMALE | 15/03/2022 | 35 WEEKS | 4weeks | 1.24 | 1.2 | *7/10 | * | 24 | 60018 | * | VAGINAL DELIVERY | 28/06/2021 | 04/04/2022 | PRIMIGRAVIDA | 9.9 | 32.4 | 75.5 | 24.5 | 3.82 | STAGE 2 ROP IN ZONE 2 WITH PLUS DISEASE | laser photocoagulation |
| 57 | 104322 | FEMALE | 20/04/2022 | 35WEEKS | 4weeks | 1.88 | 1.78 | *7/10 | RDS | 21 | 77214 | PLACENTA PREVIA | EMERGENCY LSCS | 16/08/2021 | 25/05/2022 | P2L2 | 9.4 | 32.9 | 88 | 28.9 | 3.25 | NO ROP | |
| 58 | 79772 | FEMALE | 14/04/2022 | 34WEEKS | 4weeks | 1.46 | 1.56 | *7/10 | HEART DISEASE | 35 | 75900 | BREECH PRESENTATION | EMERGENCY LSCS | 31/07/2021 | 06/05/2022 | PRIMIGRAVIDA | 10.7 | 33.2 | 82.7 | 27.4 | 3.63 | STAGE 2 ROP IN ZONE 2 NO PLUS | LASER PHOTOCOAGULATIN |
| 59 | 78022 | MALE | 16.4.22 | 35WEEKS | 4WEEKS | 1.9 | 1.88 | *6/10 | * | 22 | 76250 | * | EMERGENCY LSCS | 20/09/2021 | 27/06/2022 | P2L2 | 8.7 | 28 | 69.7 | 19.5 | 3.38 | NO ROP | |
| 60 | 87688 | FEMALE | 09/05/2021 | 33 WEEKS | 4weeks | 1.1 | 1 | *5/10 | IUGR | 20 | 82030 | PREECLAMPSIA | emergency LSCS | 17/09/2021 | 24/06/2022 | P2L2A1 | 10.2 | 32.6 | 78.6 | 25.6 | 3.68 | NO ROP | |
| 61 | 74544 | MALE | 08/04/2022 | 29WEEKS | 4weeks | 920 | 1.14 | *5/10 | * | 28 | 74047 | PREECLAMPSIA | VAGINAL DELIVERY | 11/09/2021 | 18/06/2022 | PRIMIGRAVIDA | 10.2 | 34.3 | 76.2 | 26.1 | 3.29 | STAGE 1 ROP IN ZONE 2 WITH PLUS | LASER PHOTOCOAGULATIN |
| 62 | 84824 | FEMALE | 19/05/2022 | 30 WEEKS | 4weeks | 1.4 | | *5/10 | * | 19 | 84809 | * | emergency LSCS | 15/10/2021 | 22/07/2022 | P2L1 | 9.7 | 32.4 | 75.5 | 24.5 | 3.96 | STAGE 2 ROP IN ZONE 2 | LASER PHOTOCOAGULATION |
| 63 | 67589 | FEMALE | 16/07/2022 | 29WEEKS | 4weeks | 1.7 | 1.12 | *5/10 | RDS | 22 | 107724 | * | VAGINAL DELIVERY | 24/12/2021 | 30/09/2022 | P2L2 | 9.1 | 31.1 | 75.1 | 23.3 | 3.9 | NO ROP | |
| 64 | 107993 | MALE | 17/07/2022 | 36 WEEKS | 4weeks | 3.4 | 2.78 | *5/10 | RDS | 37 | 107979 | HYPOTHYROIDISM | emergency LSCS | 12/10/2021 | 19/07/2022 | PRIMIGRAVIDA | 10.6 | 32.9 | 78.2 | 25.7 | 3.12 | NO ROP | |
| 65 | 104222 | FEMALE | 03/06/2022 | 27WEEKS | 4WEEKS | 1.07 | | *7/10 | * | 24 | 60142 | * | VAGINAL DELIVERY | 24/11/2021 | 31/08/2022 | PRIMIGRAVIDA | 10.9 | 34.4 | 80.7 | 27.7 | 3.93 | STAGE 2 ROP IN ZONE 2 WITH PLUS DISEASE | LASER PHOTOCOAGULATION |
| 66 | 100209 | MALE | 02/07/2022 | 29 WEEKS | 4weeks | 1.2 | 1.32 | *8/10 | RDS | 25 | 99757 | * | emergency LSCS | 05/12/2021 | 11/09/2022 | P1A1 | 10.9 | 34.4 | 85.9 | 29.5 | 3.69 | NO ROP | |
| 67 | 103578 | FEMALE | 08/07/2022 | 36 WEEKS | 4weeks | 2.94 | 2.78 | *8/10 | RDS | 20 | 102971 | * | emergency LSCS | 21/09/2021 | 28/06/2022 | P1A1 | 10.1 | 32.4 | 75.5 | 24.5 | 3.41 | NO ROP | |
| 68 | 11172 | FEMALE | 09/07/2022 | 30WEEKS | 4weeks | 1.95 | 1.92 | *6/10 | IUGR | 26 | 103942 | eclampsia | EMERGENCY LSCS | 07/12/2021 | 13/09/2022 | PRIMIGRAVIDA | 10.9 | 34.1 | 82.3 | 28.1 | 3.12 | NO ROP | |
| 69 | 96413 | FEMALE | 20/06/2022 | 33 WEEKS | 4weeks | 1.5 | 1.6 | *8/10 | * | 38 | 94604 | eclampsia | emergency LSCS | 26/10/2021 | 02/08/2022 | P3L3 | 9.2 | 32.4 | 75.1 | 24.3 | 3.78 | NO ROP | |
| 70 | 98562 | MALE | 09/03/2022 | 32 WEEKS | 4weeks | 1.73 | 1.6 | *5/10 | RDS | 19 | 67888 | * | VAGINAL DELIVERY | 24/07/2021 | 04/05/2022 | PRIMIGRAVIDA | 10.5 | 35.1 | 76.9 | 27 | 3.63 | NO ROP | |
| 71 | 84598 | MALE | 28/07/2022 | 33 WEEKS | 4WEEKS | 1.48 | 1.43 | *8/10 | IUGR | 26 | 113984 | * | VAGINAL DELIVERY | 06/12/2021 | 13/09/2022 | PRIMIGRAVIDA | 10.6 | 35.3 | 87.7 | 31 | 3.42 | NO ROP | |
| 72 | 897983 | FEMALE | 01/08/2022 | 35 WEEKS | 4weeks | 1.9 | 2 | *8/10 | * | 26 | 131157 | eclampsia | VAGINAL DELIVERY | 31/12/2021 | 07/09/2022 | PRIMIGRAVIDA | 10.7 | 35.2 | 81.5 | 28.7 | 3.39 | STAGE 2 ROP IN ZONE 2 IN PLUS DISEASE | |
| 73 | 124065 | MALE | 17/08/2022 | 33 WEEKS | 4weeks | 1.4 | 0.96 | *8/10 | * | 25 | 132193 | eclampsia | LSCS | NA | NA | P1L2 | 10.7 | 31.9 | 76.8 | 24.5 | 3.5 | NO ROP | |
| 74 | 124066 | MALE | 17/08/2022 | 33 WEEKS | 4weeks | 1.78 | 1.74 | *8/10 | * | 25 | 132193 | eclampsia | LSCS | NA | NA | P1L2 | 10.7 | 31.9 | 76.8 | 24.5 | 3.5 | STAGE 2 ROP IN ZONE 2 WITH PLUS DISEASE | LASER PHOTOCOAGULATION |
| 75 | 129506 | MALE | 28/08/2022 | 35 WEEKS | 4weeks | 2.32 | 2.32 | *8/10 | * | 20 | 116836 | * | VAGINAL DELIVERY | 26/11/2021 | 02/09/2022 | PRIMIGRAVIDA | 10.3 | 35.1 | 98.9 | 34.7 | 3.54 | NO ROP | |
| 76 | 122687 | MALE | 13/08/2022 | 35 WEEKS | 4weeks | 1.26 | 1.4 | *8/10 | RDS | 25 | 122493 | * | VAGINAL DELIVERY | 31/12/2021 | 07/10/2022 | PRIMIGRAVIDA | 10.4 | 33.3 | 82 | 27.3 | 3.82 | STAGE 2 ROP IN ZONE 2 WITH PLUS DISEASE | LASER PHOTOCOAGULATION |
| 77 | 95903 | MALE | 23/06/2022 | 29WEEKS | 4WEEKS | 1.3 | 1.16 | *8/10 | RDS | 22 | 95855 | TWIN PREGNANCY | VAGINAL DELIVERY | * | * | PRIMIGRAVIDA | 9.9 | 34.3 | 87 | 29.8 | 3.32 | STAGE 2 ROP IN ZONE 2 WITH PLUS DISEASE | LASER PHOTOCOAGULATION |
| 78 | 95904 | FEMALE | 23/06/2022 | 29WEEKS | 4weeks | 1.2 | 1 | *8/10 | RDS | 22 | 95855 | TWIN PREGNANCY | VAGINAL DELIVERY | * | * | PRIMIGRAVIDA | 9.9 | 34.3 | 87 | 29.8 | 3.32 | NO ROP | |
| 79 | 89822 | FEMALE | 06/06/2022 | 35 WEEKS | 4weeks | 2.24 | 2 | *6/10 | RDS | 22 | 52128 | GESTATIONAL DIABETES | emergency LSCS | 29/09/2021 | 06/07/2022 | PRIMIGRAVIDA | 10.7 | 32.9 | 78.2 | 25.7 | 3.24 | NO ROP | |
| 80 | 47520 | MALE | 30/10/2021 | 35 WEEKS | 4weeks | 1.28 | 2 | *8/10 | RDS | 25 | 48279 | eclampsia | emergency LSCS | 01/03/2021 | NA | PRIMIGRAVIDA | 10.6 | 33.2 | 82.7 | 27.4 | 3.68 | STAGE 2 ROP IN ZONE 2 WITH PLUS DISEASE | LASER PHOTOCOAGULATION |