"A ONE YEAR PROSPECTIVE STUDY TO ASSESS THE INCIDENCE, RISK FACTORS AND TREATMENT OUTCOME OF TYPE I RETINOPATHY OF PREMATURITY IN INFANTS ADMITTED TO NICUs OF KLES DR. PRABHAKAR KORE HOSPITAL & MEDICAL RESEARCH CENTRE, BELAGAVI"

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IN

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ABSTRACT

Purpose:

The purpose of this study was to determine the incidence, associated risk factors and treatment outcome of Type 1 retinopathy of prematurity (ROP) in infants admitted to the NICUs of a tertiary care centre in North Karnataka.

Methods:

This was a prospective, observational and interventional study involving the infants at-risk of developing ROP, conducted in the Neonatal Intensive Care Units (NICUs) of a tertiary care hospital in Belagavi district of North Karnataka, India. All the neonates with Birth weight (BW) ≤ 2000 gm, gestation age at birth (GA) ≤ 34 weeks & infants with BW > 2000 gm or GA 34 – 36 weeks with an unstable clinical course were included.

Results:

A total of 263 infants were screened. ROP was identified in 64 infants (24.33 %) and Type 1 ROP was seen in 28 eyes of 15 infants (5.70 %). By univariate analysis, the significant risk factors for the development of Type 1 ROP were Low GA, low BW, maternal HTN, AOP, PDA, sepsis, O2 supplementation for more than 7 days, bag & mask resuscitation, more than 5 blood product transfusion. 76.56% of any ROP cases regressed without any treatment. 23.44% developed Type 1 ROP and required treatment. 85.7% of the Type 1 ROP patients were treated with laser, 14.3% with injection and 7.1% needed both. 10.7 % needed relaser. ROP eventually regressed in all cases.

Conclusion:

The incidence of Type 1 ROP was relatively low in our cohort as compared to other studies conducted in India.

Keywords:

ROP, Type 1 ROP, Incidence, severe ROP, treatable ROP, risk factors, LASER, intravitreal injection

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LIST OF ABBREVATIONS

AOP	Apnoea of prematurity
APROP	Aggressive posterior retinopathy of prematurity
BW	Birth weight
bFGF	Basic fibroblast growth factor
CRYO-ROP	Cryotherapy for retinopathy of prematurity study
2,3DPG	2, 3- Diphosphoglycerate
ELBW	Extremely low birth weight (< 1000 gm)
ETROP	Early treatment for ROP trial
FiO_2	Fraction of inspired concentration of oxygen
FFP	Fresh Frozen Plasma
gms	grams
Hb	Haemoglobin
IGF-1	Insulin-like growth factor-1
IVH	Intraventricular haemorrhage
ICROP	International Classification for ROP
Light-ROP	Light reduction on ROP study
NICU	Neonatal Intensive Care Unit

O_2	Oxygen
OT	Operation theatre
PHPV	Persistent Hyperplastic Primary Vitreous
PDA	Patent Ductus Arteriosus
PIH	Pregnancy Induced Hypertension
PMA	Prolonged mechanical ventilation
ROP	Retinopathy of Prematurity
RLF	Retrolental Fibroplasia
RDS	Respiratory Distress Syndrome
TGF	Transforming growth factors
Transfusion	Fresh Frozen Plasma / Packed cell transfusion/Platelet
TSDL	Trans-scleral use of diode LASER
VLBW	Very Low Birth Weight (< 1500 gm)
VEGF	Vascular endothelial growth factor
WINROP	Weight, Insulin – like growth factor-1, Neonatal ROP
Wks	Weeks
YC	Yates Correction

INTRODUCTION

INTRODUCTION

Retinopathy of Prematurity (ROP) is a vaso-proliferative disorder of the developing retina in infants born premature.[1] World over, it is the leading cause of preventable blindness in children.[2]

There are approximately 285 million people who are visually impaired and 39 million blind people worldwide. This WHO estimates also shows that 80% of all the causes of visual impairments are preventable and curable. [3] Every year, about 32,000 infants worldwide become visually impaired from ROP and most of them are born in Asia.[4] A report by WHO states that India as the country with the highest number of pre-term births i.e., 3.5 million per year.[5]

In India, the incidence of ROP has been reported to be 21.6% of the screened infants and that of treatable ROP as 6.7%.[6] It has a severe social implication due to long term management.

In the context of our country, the healthcare system has advanced since the last few years. With increase in the NICU facilities at almost all the district levels, the survival rate of preterm infants and those infants with risk factors has increased, leading to more chances of infants developing ROP, but the infrastructure and skills require to be strengthened and also there is a need for developing a follow-up protocol.

Amongst the other diseases which preterm infants remain susceptible to develop, ROP holds a significant place in the causes of preventable blindness. LBW and GA at birth were observed to be highly crucial risk factors intended for the development of ROP.

The infrastructure required and the financial burden associated with it for diagnosis and management of these children is also a huge challenge in resource-limited countries such as India.

For urban areas, in conjunction with neonatological care units being outfitted with the state-of-the-art technological environment and extremely competent personnel delivering best possible care of extremely immature newborns, ROP occurrence is on a climb. By early recognition and well-timed intervention, loss of sight due to ROP is escapable.

The intent of this research is to have knowledge of the incidence of treatable (Type 1) ROP, to associate it with maternal and neonatal risk factors and to study the treatment outcomes of newborns discharged from the neonatal care units of Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi

KLES DR. Prabhakar Kore Hospital & MRC is a tertiary care referral centre for the care of high-risk newborns for North Karnataka. The number of surviving extreme preterm newborn with multiple risk factors has improved over last decade due to optimal infrastructure and standardizing care.

AIMS & OBJECTIVES

AIMS AND OBJECTIVES

Primary Objective:

To find out the incidence of Type 1 ROP in infants at risk for ROP.

Secondary Objectives:

1. To study the risk factors for the development of Type 1 ROP.

2. To study the treatment outcomes.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

HISTORY

RETINOPATHY OF PREMATURITY (ROP) is an iatrogenic illness seen in the infants born premature.

It was designated "retrolental fibroplasia" (RLF) in reports of Theodore L. Terry[7] after his observations on the proliferation of the embryonic hyaloid system occurring retrolentally. He also stated its connection with premature birth. He investigated the unilateral pathological specimens (most seemingly PHPV) and presented details which he thought to be similar to bilateral cases of retrolental fibroplasia.

He postulated that "some new factor has arisen in extreme prematurity to produce such a condition" and he argued that this new factor was 'excess light'.

Heath coined the term ROP in 1951. In 1951, Dr Kate Campbell[8] noticed that excess oxygen administration in infants lead to toxic effects and RLF and there was a lower incidence when less oxygen was administered. She concluded that "normal oxygen environment of the newborn full-term infant is abnormal for the premature infant". More satisfying evidence showed up in 1952 by Crosse and Evans[9] who remarked that decreasing the duration of oxygen treatment decreased the incidence of RLF. It was also seen in one randomized trial by Patz *et al*.,[10] and in a cooperative trial by Kinsey *et al*.,[11] in 1956.

Two epidemics of ROP occurred in the developed countries in the last 60 years. The first epidemic occurred in 1940-1950. Controlled use of oxygen later lowered the proportion of blindness. Despite careful monitoring of oxygen supply, there was a comeback in the increased number of cases of ROP during 1970-80 and thence, a second epidemic of ROP was registered while it was also noted that, a greater percentage of ELBW- infants survived in industrial developed countries.[12–14]

Phelps[15] in 1981 estimated the incidence of ROP associated with an increase in the survival rates of infants weighing less than 1000gms at birth.

In 1970s Nagata treated the ridge and adjacent avascular retina[16]. Hindle and Leyton, treated the ridge, and the retina anterior and posterior to it. McPherson, Hittner, and Kretzner[17] advocated cryotherapy of the ridge and adjacent avascular zone to destroy the spindle cells, which were presumed to be the source of angiogenic factor.

The International Classification of ROP was devised in 1983 under the command of John Flynn[18].

With the advances in healthcare system and of telemedicine to aid in ROP screening and diagnosis and laser photocoagulation replacing cryotherapy as the standard mode of treatment, more babies are being screened, diagnosed, and treated earlier.

INCIDENCE

ROP occurs worldwide omitting countries with high infant mortality rate (IMRs) where the infants do not survive. With advances in perinatal medicine, the survival rate in ELBW infants has increased from 5% to 78% in the last 50 years, while in VLBW infants, it has increased from 35% to 90%. But the increase in survival rates in these infants has led to increase in morbidity thence provided a situation favouring increase in the incidence of ROP.

In CRYO-ROP study, the incidence of the disease in a group of premature infants born with birth weights <1251gms was 65.8% and in infants <1000gms it was found to be 81.6%[19]. In the ETROP study done 15 years later, the incidence of ROP in infants <1250gm was found to be 68%. The incidence of more-severe ROP (pre-threshold) was 36.9% among infants with ROP in ETROP Study but in CRYO-ROP study it was 27.1%[20].

A review of literature reveals that the incidence and severity of ROP increases with decreasing gestational age at birth and birth weight. The occurrence of ROP in studies elsewhere India demonstrated an incidence of 9.4%-38.9%[21–25]. A review of literature from the Indian subcontinent reveals the incidence to be 17.5%-46%.[26–30]

Studies from the developing countries show that, though the trend in ROP was not similar in all units, there is an overall reduction in the incidence of ROP whenever there is any ongoing surveillance programme. It has been noted that prevalence of severe ROP (Threshold disease) is on the decline. A study conducted by Aggarwal and co-workers over 7 years found a drop in the incidence from 46 to 21%.[30]

In a multicentre study conducted in the UK, a statistically significant decrease in incidence of ROP was found in infants weighing more than 1250gm[31].

Table 1: Incidence of ROP in Indian and International studies

INCLUSION CRITERIA			
INDIAN STUDIES	**GA (weeks)**	**BW (grams)**	**Incidence**
Rekha[27],1996	≤ 34	< 1500	46 %
Maheshwari[28],1996	< 35	< 1500	20 %
Patil[29],1997	< 32	< 1250	17.5 %
Aggarwal[30],2002	< 35	< 1500	20 %
Gupta[32], 2003	≤ 35	≤ 1500	21.7 %
Nair[26],2003	≤ 32	< 1500	25.4 %
INTERNATIONAL STUDIES			
Hussain[33],1999	< 32	< 1500	21.3 %
Fledelius[23],2000	< 32	< 1500	9.4 %
Blair[24], 2001	< 30	< 1250	38 %
Conarth[34],2004	≤ 32	< 1750	10 %
Shah[21],2005	≤ 35	< 1500	29.2 %
Fortes[35],2007		≤ 1000	48.9 %
		≤ 1500	18.2 %
Binkhathlan[36],2008	< 36	< 2000	56 %

PATHOGENESIS

NORMAL RETINAL VASCULAR DEVELOPMENT

The vascular system in the human eye has two components, the Retinal vascular system, and the choroidal vascular system. It develops by the process of vasculogenesis[37] from the precursors, which migrate from the deep layers of the retina to the inner retinal surface and form the angioblasts.

At around 6 weeks of gestation, the hyaloid artery, which is a remnant of primitive dorsal ophthalmic artery, grows forward till the posterior pole of the lens. Till 16 weeks of gestation, choroidal vessels alone provide nutrition to the inner as well as the outer retina but the inner retina remains avascular practically.

The retinal vascular system starts developing at 16 weeks GA from the hyaloid artery adventitia, in the form of "spindle cells" from its mesenchyme. These cells further migrate towards the periphery till they reach the ora serrata.[38]

In addition, Muller cells and ganglion cells are also found to be important in retinal vascular development.[39–41] The spindle cells advance at a rate of 0.1mm/day, reach the nasal ora by 36 weeks and by 40 weeks they reach the temporal ora.

PATHOGENESIS OF ROP

In utero, the estimated oxygen supply to the fetus is about 30-40 mm Hg. At birth, there is transformation of oxygen source from the placenta to the lungs thereby raising the saturation levels from mixed venous to arterial levels which is about 60 – 100 mm Hg.[42] So the environment after birth is relatively hyperoxic, especially when oxygen is used for resuscitation.[43] however the lungs of the fetus, being immature, are not efficient to handle transfer of higher saturation of oxygen.

So, there is an initial hyperoxic state due to change of oxygen source from mixed venous arterial; additional inspired O_2; unformed unharmed lungs; and a minimal rate of retinal metabolic O_2 utilization.

Post-natal, this state of relative higher O_2 starts to alter. The alveoli get injured, the alveolar – blood O_2 swap is conceded, and there is rise in retinal metabolic need for O_2 according to the programmed embryological events giving rise to a state of comparative hypoxia. This switch is not slick but a straight one.

Angiogenic factors like vascular endothelial growth factor (VEGF) play a crucial role in the retinal vascular system development. VEGF is an oxygen-regulated factor produced by astrocytes in response to tissue hypoxia in the avascular retina. Its transcription is stimulated by hypoxia and suppressed by hyperoxia.[44] The state of hypoxia causes an up-regulation of VEGF and the state of hyperoxia causes down-regulation of VEGF. Other important angiogenic factors are IGF-1, bFGF & TGF associated with retinal vascularization.[45–49]

IGF -1 is a non–oxygen-dependent factor recently found to be deficient in premature infants who later develop ROP.[50] Studies suggest that the degree of severity of ROP correlates to the serum level IGF-1 in premature infants.[42] It controls VEGF activation, hence acts synergistically.[44] IGF-1 is required for survival of the vascular endothelial cell.[42]

Two important hypotheses have been described:

a) *The Classical Theory*:

Proposed by Ashton and Patz[51]. States that elevated arterial PO_2 causes retinal vasoconstriction, leading to vascular closure and resulting in permanent vascular occlusion. Adjacent to closed capillaries there occurs endothelial cell proliferation when neonate returns to room air, leading to neovascularization. The subsequent extension of which may reach vitreous, producing haemorrhage leading to fibrosis, vitreous traction and retinal detachment.

b) *Spindle Cell Theory*:

Proposed by Kretzer *et al*.,[52] states that the induction of retinal and vitreal neovascularization occurs due to spindle cell insult. After birth, when the spindle cells are exposed to hyperoxic environment because of increased oxygen diffusion through the thin and avascular peripheral retina, free radical formation occurs, which attack the compromised spindle cells having deficient anti-oxidative defence mechanism. These abnormal spindle cells stop migration and canalization and lead to neovascularization at the shunt site.

ROP occurs in two phases:

1.**Phase I** :(Vaso-obliteration phase) 21 – 31 Weeks

Phase of decrease or cessation of vascular growth.

Factors responsible include:

a) Arterial oxygen (60 – 100 mm Hg).

b) Increased FiO_2 (21 %).

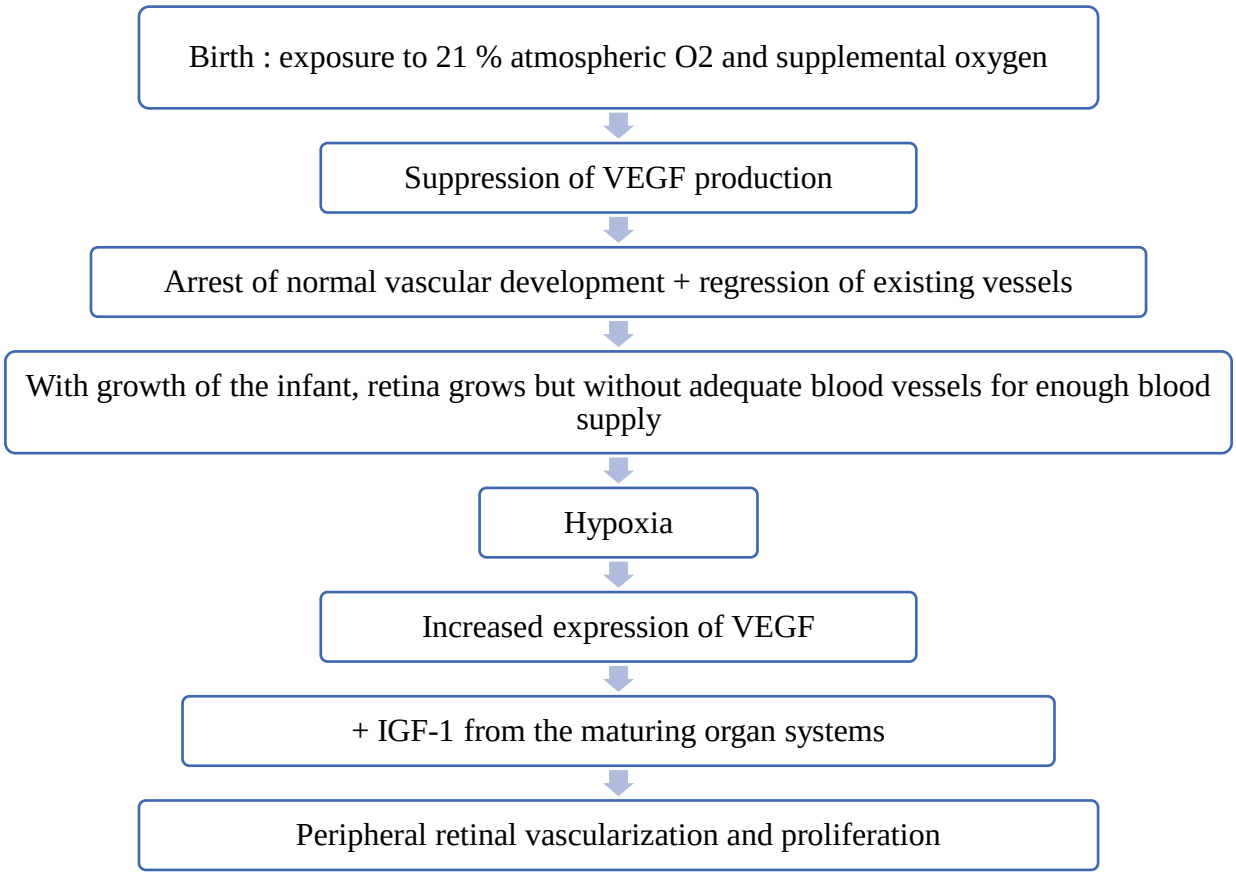
c) Little retinal O_2 consumption secondary to truncated metabolism.

All merge to produce comparative hyperoxia and lead to cessation of vascular growth and regression of developed retinal vessel proliferation

2. **Phase II** (Vaso-proliferation phase) 31 – 41 Weeks

Phase I leads to hypoxia leading to abnormal vessel proliferation.

Flowchart 1: Pathogenesis of Type 1 ROP



RISK FACTORS FOR DEVELOPMENT OF ROP

Retinopathy of prematurity is a multifactorial disease. Based on all the clinical and epidemiological studies, numerous risk factors have been proposed.

Definite risk factors:

- Prematurity / Gestational age
- Birth weight
- Oxygen supplementation

Associated risk factors:

- Light
- Apnea / Bag & Mask resuscitation
- Respiratory distress syndrome
- Asphyxia / Hypoxia
- Sepsis
- PDA / treatment with Indomethacin
- Blood transfusions
- Intraventricular haemorrhage
- Maternal factors - Anaemia

BIRTH WEIGHT and ROP

India has the third-highest incidence of LBW infants, with 0.4 million <1500 g and 1.7 million infants weighing <2500 g.[53]

CRYO-ROP was amongst the first studies to correlate the birth weight and incidence of ROP in premature babies with an incidence of 65.8% in babies with birth weight <1251gms and 81.6% for babies with birth weight less than 1000 g[19]. In this cohort, every 100gm surge in BW had cut the chances of attainment of severe ROP by 27%.

ETROP study done in 2001 showed an overall occurrence of ROP to be 68% in babies with birth weight <1251 grams. A study done by Fledelius *et al*., found a statistically significant decrease in incidence of ROP in infants weighing more than 1250gm[23]. Gupta[32] and co-workers found no cases of ROP in babies weighing more than 1250gm.

A review of literature reveals that the incidence and severity of ROP increases with decreasing gestational age and birth weight.[22,25]

Contrary to these reports, in a retrospective study done by Anand Vinekar *et al*., [54] showed that severe ROP was encountered in babies weighing > 1250 g at birth in developing countries and suggested that, the western screening guidelines may require modifications.

Recent Indian guidelines suggest screening of all infants with birth weight < 2000gm and also those with a higher birth weight if they were born at < 34 weeks.[55]

OXYGEN AND ROP

The finding of the relation between oxygen with ROP dates to 1951 when Campbell noted that those infants who were administered less oxygen had a lesser incidence of RLF. It has been proved to be one of the main risk factors for the development of ROP.

During the short transition period between placental and lung oxygenation, the retina probably undergoes frequent swings of hyperoxia and hypoxia. The sickest infant has the most volatile transition phase of retinal oxygenation. It suggests that the mismatch between supply and need for Oxygen as the ultimate cause of ROP.

A study by Kinsey *et al*., stated that "RLF is associated with concentration of oxygen administered in the lightest birth weight group, but the strongest association, aside from birth weight, was with time in oxygen." [56]

Surfactant Positive Airway Pressure and Pulse Oximetry Trial (SUPPORT) randomized controlled trial was conducted in babies born with gestational ages between 24 to 27 weeks, monitored their SpO2 till the age of 36 weeks post menstrual age and concluded that "Among extremely preterm survivors to discharge, the association between SpO_2 and severe ROP depended on the timing and duration of oxygen supplementation."[57]

Gunn analyzed data from infants born with birth weights between 501 and 1500 gm and who survived and noticed a substantial association amid the spartan grade of cicatricial disease and the period of O_2 treatment[58].

A study by co-operative study group concurred with the findings of this group. In this study, Kinsey *et al*., emphasized on the strongest association of birth weight and also time of oxygen with occurrence of ROP.[56]

A study by Rowena *et al*., concluded that " Implementation of graded SpO2 targets decreased severe ROP and need for laser therapy, without increasing mortality."[59]

A study by Meaoyung states that "O_2 saturation levels must be supervised and retained under 95% to avert reactive oxygen species-related illnesses, like ROP and bronchopulmonary dysplasia"[60]

A study led by Mnghua *et al*., stated O_2 exposure at 28 days to emerge as a significant risk factor for ROP.[61]

They observed that infants who were put on 91% - 96 % SpO2 for at least 2 weeks in the first 1 – 5 weeks postnatally were associated with increased odds of severe ROP. Also, the infants who were put on 97% to 100 % SpO2 at 6 – 9 weeks postnatally were at a higher incidence of severe ROP.[57]

APNOEA

In their study, Kim *et al*.,[62] found apnoea to be an independent risk factor for development of ROP and also as a significant factor that worsened pre-existing ROP.

An increased incidence of hypoxemia and apnoeic episodes requiring bag and mask ventilation was found among infants with severe ROP, than in a control group[30,58].

The study by Rajiv *et al*., showed the efficient management of apnea to be crucial in minimizing the risk of ROP.[30]

In their study, Chen *et al*.,[63] found apnoea more than 20 sec to be an independent risk factor for developing Type 1 ROP.

HYPOXIA

Szewczyk[64] suggested that too rapid reduction of oxygen level after a child had been habituated to an enriched oxygen atmosphere resulted in ROP. He found that it could be treated by re administering high oxygen to the infant then to be followed by slow return to atmospheric air. He said that "ROP was a result of hypoxia and not due to oxygen toxicity."

Cohen and co-workers found an association of ROP with hypoxia along with other abnormal neurological signs and that 14% were having anoxia in the immediate postnatal period.[65]

Katzman *et al*., reviewed the neonatal course of 50 infants who developed ROP and found that there was no significant difference in the duration of oxygen therapy, exposure to different concentrations of oxygen when those with stages III to V disease were compared with those with Stages I to II disease[66]. They did, however, find that the more severe stages were associated with significantly more hours spent with arterial PO2 levels below 35 mmHg.[67]

Shohat *et al*., also reported similar results among infants weighing <l,250gm.[68]

RESPIRATORY SUPPORT (VENTILATOR / CPAP)

PMA is described as " Ventilator dependency for >7 days" is the commonly recognized risk factor for ROP.[69–79]

A study by Ying *et al*., included 979 infants who needed respiratory support and revealed that mechanical ventilation is an independent risk factor for developing significant ROP.[80]

Several studies have found that the requirement for CPAP likewise raises the probability of developing ROP,[21,22,25,81] and delays involution of ROP.[82]

SEPSIS

Sepsis has been found to be an independent risk factor for the development of ROP.[22,25] It may act through endotoxins and cytokines or by the oxidative burst occurring in the neutrophils in response to infection. The prevention of these events and its early control could reduce the incidence of ROP.

Agarwal *et al*., reported blood cultures to be positive in 67 % of infants who developed ROP. [30] Liu PM *et al*., in her study, found sepsis as the most significant factor contributing to development of ROP.[83]

Mittal *et al*., found that "Candida sepsis is independently associated with increased severity of ROP and the need for laser surgery in extremely low birth weight infants." [84]

A study done by Parupia H *et al*., found that, "the risk of threshold ROP requiring laser treatment was higher in infants who developed fungal sepsis."[85]

A systematic review by Huang *et al*., showed that neonatal sepsis had escalated the risk of both any stage ROP as well as severe ROP in particular.[86]

ANTENATAL STEROIDS

Use of steroids antenatally has been indicated to lessen the illness and death rate amongst neonates born prematurely. But the effect it has on ROP has always remained controversial.

A study by Yim *et al*., concluded that "Antenatal steroid administration is associated with a reduced risk of ROP development and progression to severe ROP."[87]

A study by Higgins *et al*., concluded that "Antenatal dexamethasone administration appears to be associated with a decreased incidence of development of ROP of stage 2 or higher."[88] Maini *et al*., stated that "Antenatal betamethasone may be preventive for severe ROP."[89]

A study by the INDIAN ROP study group concluded that "ANS prophylaxis protected both against ROP development and against severe forms of ROP."[90]

MODE OF DELIVERY

Manzoni *et al*., had studied the incidence of threshold ROP in 174 infants and found the incidence of threshold ROP to be 26.4% of which 40.9% were delivered vaginally and 17.5% were delivered by cesarean section.[91]

Studies by Abdel *et al*.,[92] Seiberth *et al*.,[93] found no significant relationship between the mode of delivery and occurrence of ROP. This was in variance with a study by Shah *et al*.,[21] who found that Cesarean section delivery was significantly associated with occurrence of ROP.

MATERNAL DIABETES

Maternal diabetes causes maternal hyperglycemia which in turn causes fetal hyperglycemia.

A study by Opara *et al*., concluded that "Maternal diabetes is associated with ROP and the strength of association increased with increasing severity of ROP."[94]

MATERNAL HYPERTENSION

Maternal pre-eclampsia causes chronic intrauterine stress, as a statistically independent factor and as having an influence on the incidence of ROP.[93]

Shah *et al*., in their study found maternal pre-eclampsia to be a major component in developing severe ROP.[21]

A recent study on the Hypertensive diseases in pregnancy and ROP included around 45,082 infants and it concluded that there was no clear association, attributing to a variable quality of the study and various other probable perplexing factors like the related maternal circumstances besides the postpartum O_2 therapy.[95]

PPROM

PPROM was defined as "the presence of vaginal pooling with either documented nitrazine positive testing or ferning prior to regular uterine activity." The results have been controversial in different studies.

In a study by Lee *et al*., it was found to be associated with reduced risk of plus disease and pre-threshold / threshold disease.[96]

In a study by Ozdemir *et al*., PPROM >18 hrs was found to be an independent risk factor for development of severe ROP requiring treatment.[69]

Swedish research on WINROP system observed that PPROM has got shielding effect in severe ROP of Stages ≥3.[97]

HYPOCARBIA AND HYPERCARBIA

Hypercarbia i.e., high levels of CO_2 in the blood prevents the vasoconstriction of vessels in the retina which is body's primary response to high oxygen levels i.e., hyperoxia as the retina might then be exposed to damaging effects of high levels of oxygen in the blood as proposed by Bauer and Widmayer.[98]

Walbarsht *et al*., proposed that high levels of oxygen may be causing defective removal of CO_2 from the retinal tissue resulting from constriction of the retinal arterioles with decreased perfusion and from its interference with the binding of haemoglobin to CO_2 when haemoglobin in the retinal venous circulation is approximately 100% saturated with O_2. Both these leading to CO_2 accumulation further leading to retinal vasodilatation which further leads to proliferation of retinal vessels causing ROP.[99]

Several other studies found no clinical relation between higher pCO_2 and the development of ROP.[68,100] A study by Balazs Gellen *et al*., noted that "Neither variable blood carbon dioxide tension nor duration of hypercarbia or hypocarbia in the first 2 weeks of life was associated with the development or severity of ROP."[101] Comparable outcomes have been noted in a research by Liao SL et.*al*., during the first 3 days.[102]

A study by Shohat *et al*., found "significant association to be present between hypocarbia and the development of severe ROP i.e., an increased frequency of episodes of hypocarbia ($PaCO_2$ <25) and alkalosis (pH>7.55) among infants developing ROP."[68]

INTRAVENTRICULAR HAEMORRHAGE

IVH is a crucial impediment seen in prematurity causing neurodevelopmental delay.[103]

"IVH appears in around 25–30% of infants who are <1,500gms and born preterm."[104] IVH has been correlated with ROP.

Sajjadin *et al*., reported IVH in 64.4% of infants with any stage ROP.[105]

Procianoy *et al*., found that "IVH was the only condition significantly correlated with ROP. It was proposed that as cerebral and retinal circulations respond similarly to changes in PaO_2, $PaCO_2$ and blood pressure and the two conditions might be caused by a common mechanism."[25,25,106]

MULTIPLE PREGNANCY

It is connected to preterm births, smaller weight at birth, morbidities which may affect risk for developing ROP.[107]

CRYO-ROP trial demonstrated that infants born of single pregnancy were having a lesser risk of ROP than twins/multiples.[108] Similar results were also obtained by other studies.[70,71,109–114]

Several studies have reported a high incidence of ROP in single pregnancy,[115] few studies also showed no much difference between both singleton and multiple births[115,116]

This variation might have occurred because of the differences in the mode of delivery and many other factors.

ANAEMIA AND BLOOD TRANSFUSION

Following blood transfusion, the tissue oxygen levels are increased, causing reduced affinity to oxygen by adult haemoglobin, unlike fetal haemoglobin (HbF).

Another theory is that following blood transfusion, there is an increase in the free iron load in the blood, causing damaging effects on the retina via various intermediates of oxygen, resulting in the generation of extremely responsive oxygen radical.

Usually, safeguard against unbound iron is offered by ceruloplasmin along with transferrin, but in preterm infants with GA < 34 weeks, the concentrations of the binding proteins are extremely low, leading to swift saturation of transferrin.[117,118]

Studies done in the past have emphasized the role of blood transfusions and iron intake on the development of ROP[117,118].

A study by Nugud *et al*., in 2019 concluded that "The key factors associated with ROP, are intracranial haemorrhage with or without neonatal seizures and a high frequency of blood transfusions."[22,119] Articles have given different viewpoints on the role of transfusions. Few reports suggested anaemia itself as a possible factor for ROP, while others stated that a superior percentage of hematocrit and repeated blood transfusions are crucial individual risk factors.[120–122]

A study done by Stutchfield *et al*., to identify association between HbF and ROP concluded that "Replacing HbF by HbA during transfusion may promote ROP development by rapidly increasing oxygen availability to the retina. Conversely, maintaining a higher % HbF may be a protective factor against ROP".[123]

A study done by Akter S *et al*., stated, "Frequent blood transfusion causing substantial accumulative volume, transfusion in the first week of life has considerable correlation with ROP."[124]

Thrombocytopenia:

Platelets have damage recovery function. Also, they remain watchdogs of angiogenesis. They accumulate, transfer and release factors of angiogenesis like VEGF, augment or hinder local angiogenesis by sticking to endothelium.[125,126] Numerous researches noted correlation amongst thrombocytopenia coupled with severe ROP as well as APROP[127] besides Posterior pole ROP.[128]

A study done by Vinekar *et al*.,[129]and a study by Lundgren *et al*.,[127] showed " Platelet numbers of infants with APROP was substantially lesser than the controls."

RESPIRATORY DISTRESS SYNDROME

RDS is set off due to surfactant insufficiency in newborn. It marks the development of hypoxia in the infant which further requires oxygen therapy and mechanical ventilation. Both of these factors are associated with increased risk of developing ROP.[90,130–138]

Surfactant is given as a treatment of RDS. Several studies were conducted in different countries to find the association between surfactant and ROP and concluded that surfactant therapy is an independent risk factor for developing ROP in the infant.[22,71,72,136,139]

In his study, Repka concluded that "the widespread use of prophylactic surfactant therapy, will not change the incidence of retinopathy of prematurity in extremely low-birth-weight infants.

However, the absolute number of affected patients will likely increase because of the decrease in mortality of extremely low- birth-weight patients, the patients most at risk for retinopathy of prematurity. Though, surfactant substitution therapy might be beneficial to developing cicatricial, brutal ROP."

PATENT DUCTUS ARTERIOSUS(PDA) AND TREATMENT

A study by Tsui *et al*., concluded that "PDA and indomethacin were associated with plus disease and ROP requiring treatment on univariate analysis, but this was not significant after adjusting for other risk factors. PDA was also strongly related to bronchopulmonary dysplasia and blood transfusions, which may explain its effect on ROP."[140]

A study by Weisz *et al*., stated that "A period of conservative management after failure of medical PDA closure may be considered to reduce the number of infants treated with surgery." As they found that incidence of ROP increased post ligation of PDA.[22,25,141]

ROLE OF DEXAMETHASONE

Dexamethasone has been used for improvement in premature infants with poor respiratory compliance. The effects of administering dexamethasone early in persistent lung illness and pulmonary mechanics upon ROP development in VLBW infants have been studied.

Durand *et al*., studied the same in VLBW infants and reported "an improved respiration in terms of lung compliance and increased tidal volume. It reduces FiO_2 and mean pressure in the airway, also facilitates extubating, lessens the period of mechanical ventilation."[142]

Higgins *et al*., found that antenatal dexamethasone administration to be associated with decreased incidence of ROP of stage 2 or higher.[88] A study by Parupia *et al*., concluded that "Postnatal corticosteroid use is an independent risk factor for development of ROP. The risk of threshold ROP requiring laser treatment was higher in infants who developed fungal sepsis"[85]

A study by Doyle *et al*., stated that "While early corticosteroid treatment enables extubation besides reducing the risk of bronchopulmonary dysplasia and PDA, it has brief side effects which could be severe. Certain studies with a long-term follow-up reported an enhanced risk of unusual findings on neural examination along with an increased risk of cerebral palsy."[143] Hence, early use of corticosteroids should be warranted with caution.

LIGHT AND ROP

The LIGHT-ROP Study, a prospective, randomized, clinical trial conducted in 409 premature infants was designed to determine if any reduction in the ambient light exposure to premature infants eyes would cause any reduction in the incidence of ROP.[144] The study showed that the reduction in ambient-light exposure did not alter the incidence of ROP.

A study by Christine *et al*., concluded that "Decrease in ambient light exposure in NICUs is not of advantage in plummeting the incidence of ROP."[145]

Ackerman *et al*., in his study, compared the incidence of ROP amongst infant's eyes exposed to natural lighting with that of eyes exposed to reduced lighting and found no difference in incidence and severity of ROP in premature infants.[146]

Eliane *et al*., in a study, concluded that "Bright light is non-causative for ROP and that the decrease in exposure of the retinas of premature infants to light has no consequence on the occurrence of the disease."[147]

VITAMIN E DEFICIENCY

Vitamin E is a fat-soluble vitamin and an antioxidant. It can scavenge free radicals derived from oxygen.

The retina in the premature infant is defenseless to the lethal properties of these O_2 derivative-free radicals. Thereby prophylactic vitamin E has been suggested for the management of ROP.[148]

There have been three clinical trials[149–151] to document the efficacy of supplementation of Vit E in defeating the progress to severe ROP.

The spindle cells, which are the mesenchymal precursors of the inner retinal capillaries, have been proposed to be the primary inducers of the neovascularization associated with ROP. Exposure of these mesenchymal precursors to elevated oxygen tension increases their gap junction area, halting the usual vaso-formative course, ultimately triggering neovascularization which is detected 8–12 weeks later clinically.

Vit E complementation over the short plasma levels in these infants[152] defeats gap junction formation, reducing the severity clinically, minus shifting the over-all occurrence of ROP.

OTHER RISK FACTORS ASSOCIATED WITH ROP

Several other factors have been implicated in the development of ROP in premature infants. Defining the role of these factors in the presence of other major factors, like LBW and early GA, is again insignificant. Since oxidative injury leads to ROP, few studies have stated bilirubin to be an important antioxidant present physiologically. A recent study found that there was no definite correlation concerning bilirubin levels coupled with severe ROP.

Dopamine is used in managing hypotension in high risk infants born prematurely. It has been correlated with enhanced risk for the developing threshold ROP. Hence, extra importance on examination of high-risk infants necessitating dopamine therapy, for treatment of hypotension is vital.[153]

A study was done by Papp *et al*., and they observed "infants having active ROP to be having least reduced glutathione (GSH), greatest oxidized glutathione (GSSG), maximum GSSG/GSH ratio. The glutathione redox ratio remained acceptable as a biological monitor for detecting active ROP amongst infants born premature."[154]

CLASSIFICATION OF ROP

There were many classification systems used before 1980, which relied on the system proposed by Reese *et al*., in 1953 and included classifications by Majima, Kingham, Quinn *et al*. Schaffer *et al*., and Mc-Cormick.

ICROP was proposed[18] by an international committee of 23 ophthalmologists from 11 countries in 1984 and was expanded in 1987[155].

The ICROP classification was revisited in 2005[156] by 15 ophthalmologists from 6 countries to include aggressive posterior ROP, pre-plus disease and also to clarify the extent of Zone I.

It retained descriptions under three aspects of the original ICROP: location, extent and severity.

Classification contains the following five components:

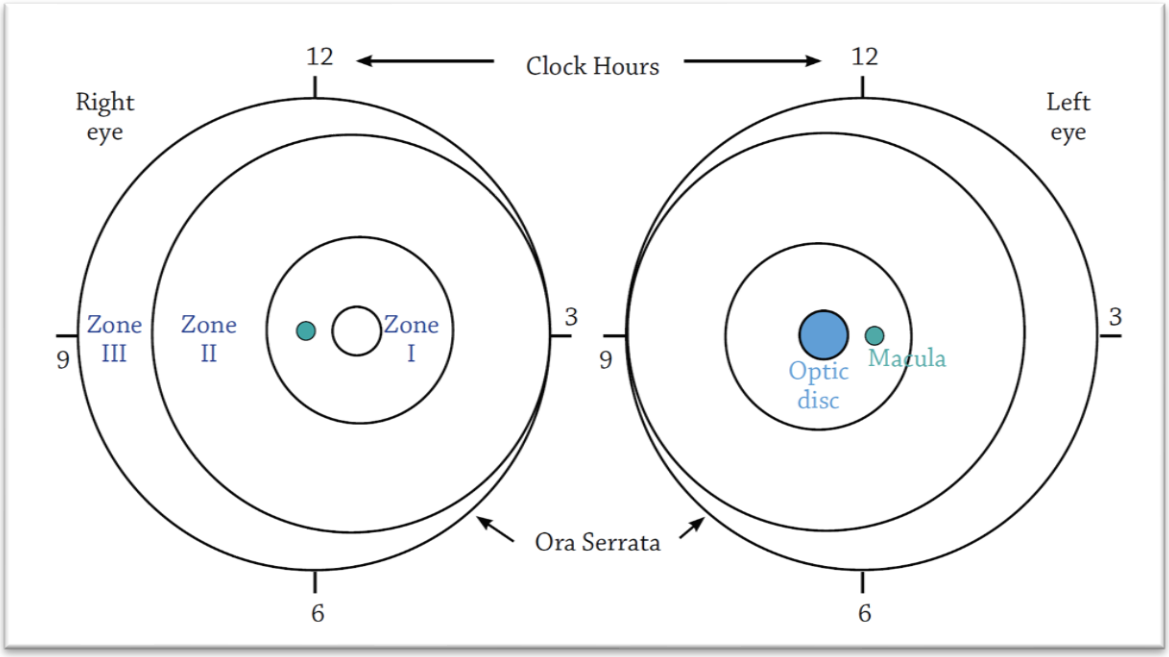
Location

Zone I : Formed by an imaginary circle drawn with the optic nerve as the centre and twice the distance from the centre of the optic nerve to the macula as the radius.

Zone II : A doughnut-shaped area outside Zone I, with a radius extending from the edge of zone I to the equator on the nasal ora of the retina.

Zone III : A crescent-shaped area lying outside Zone II temporally from the edge of Zone II till the temporal Ora Serrata.

Figure 1: Scheme of the retina showing Location and Extent of ROP



Extent

It refers to the location of the disease circumferentially and is reported in clock hours or 30° sectors in the appropriate zone.

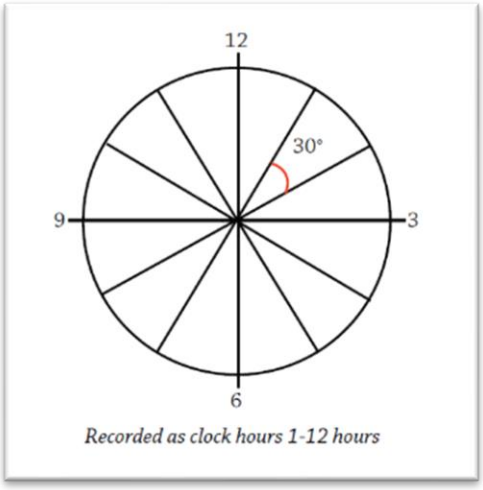


Figure 2: Scheme showing clock hours of the retina

Staging

Stage 1

A **demarcation line** is a thin white line that separates the normally developed retina from the undeveloped avascular retina.

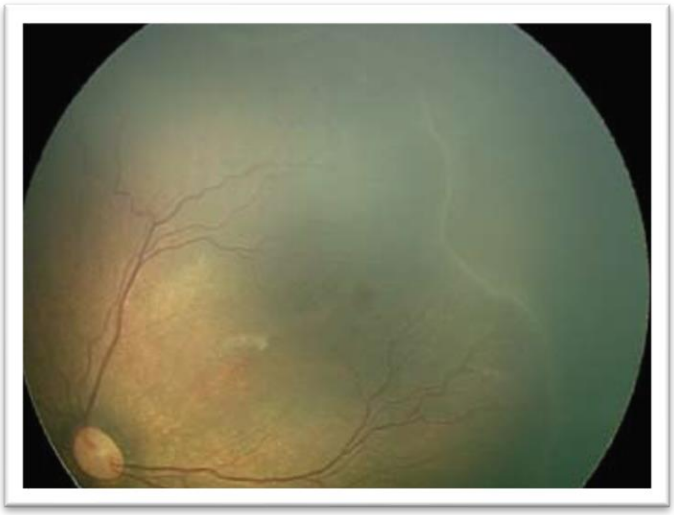


Figure 3: Demarcation line

Stage 2

A **ridge** is a scar tissue that has height and width and replaces the line of stage 1 and extending inward from the retinal plane.

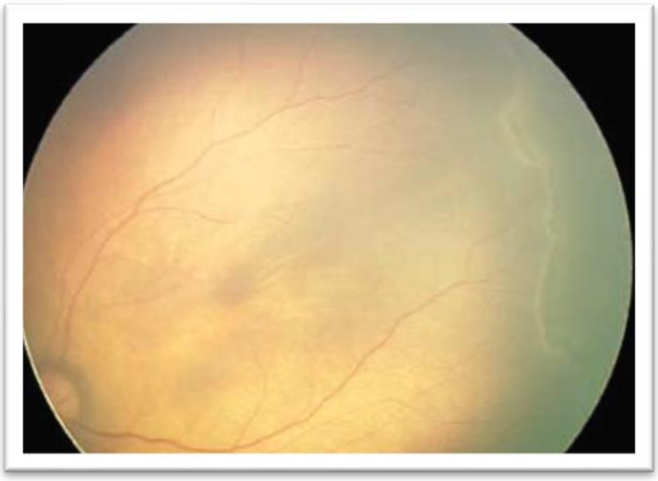


Figure 4: Ridge

Stage 3

In this stage, there is **fibrovascular proliferation** from the ridge over the retina and beyond the surface onto the vitreous. The abnormal blood vessels and fibrous tissue develop on the edge of the ridge extending into the vitreous.

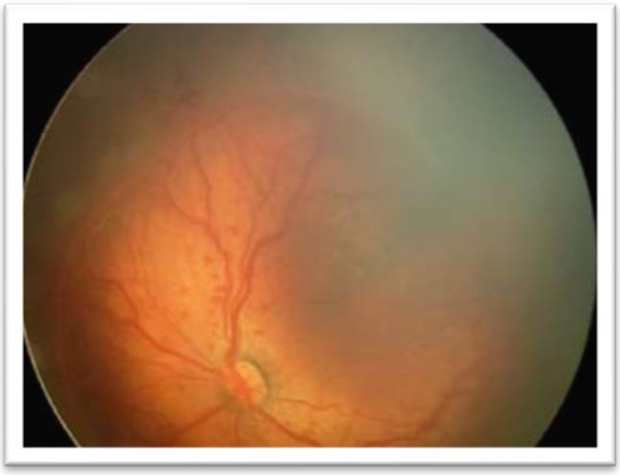


Figure 5: Extra retinal fibrovascular proliferation

Stage 4

There is partial detachment of the retina which may result from the pull of scar tissue on the retina.

Stage 4A: Partial detachment without involving the Macula.

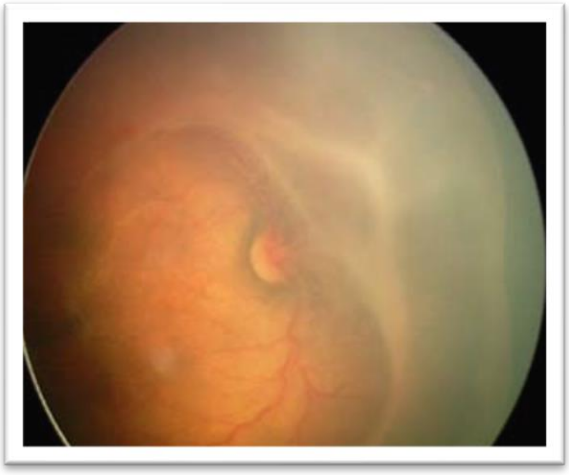


Figure 6: Partial Retinal detachment without involving the Macula

Stage 4B: Partial detachment involving the Macula.

Figure 7: Partial detachment with macula

Stage 5:

Complete retinal detachment occurs making the retina assume a funnel shape. It is described as open or narrow in the anterior and posterior regions.

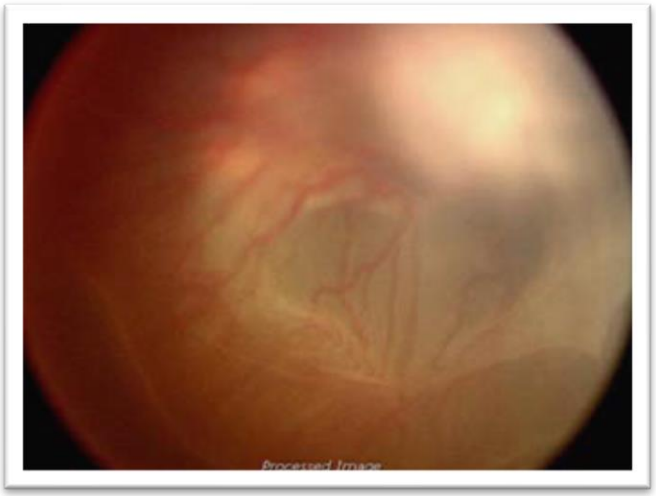


Figure 8: Total retinal detachment

Plus Disease

It refers to the presence of vascular dilatation and tortuosity of the posterior retinal vessels and indicates a severe degree of ROP and may be associated with iris vascular engorgement, pupillary rigidity, and vitreous haze.

ETROP study has used clinical photographs as reference to define plus disease and defined plus disease as dilatation and tortuosity in more than or equal to 2 quadrants. [157]

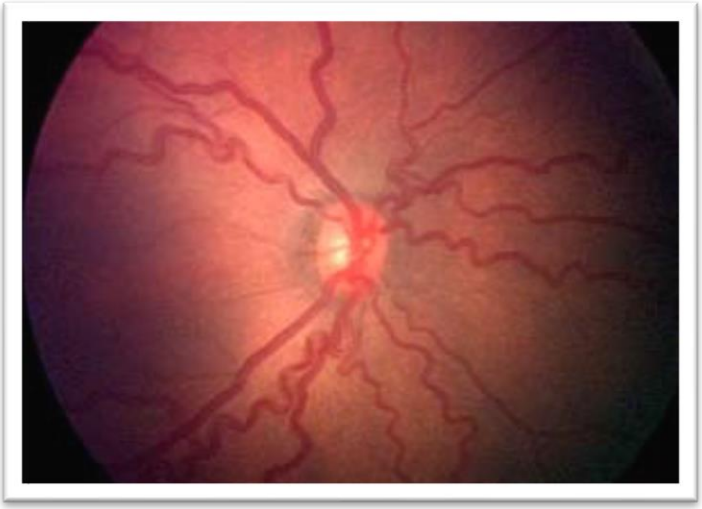


Figure 9: Plus disease

Pre-plus disease

It is defined so when there are vascular abnormalities of the posterior pole but they are insufficient for the diagnosis of plus disease.

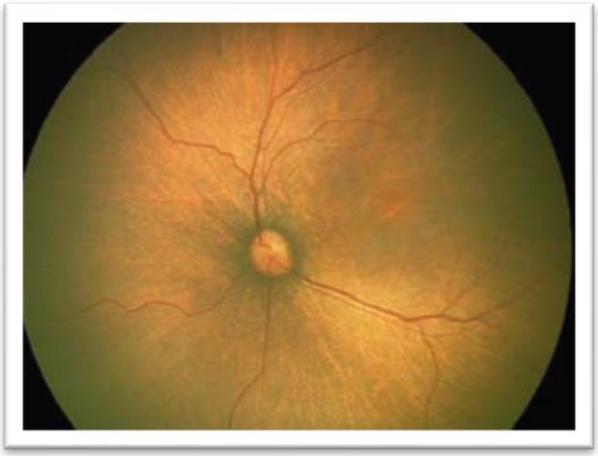


Figure 10: Pre-plus disease

Aggressive posterior ROP (AP-ROP):

It is a severe form of ROP both in progression and severity. If untreated, it progresses to stage 5 ROP. The characteristic features include its posterior position, distinction of plus disease, along with the poorly typified nature of the retinopathy. It might not have a typical ridge or extraretinal fibrovascular spread and it might not follow the regular course of progression.

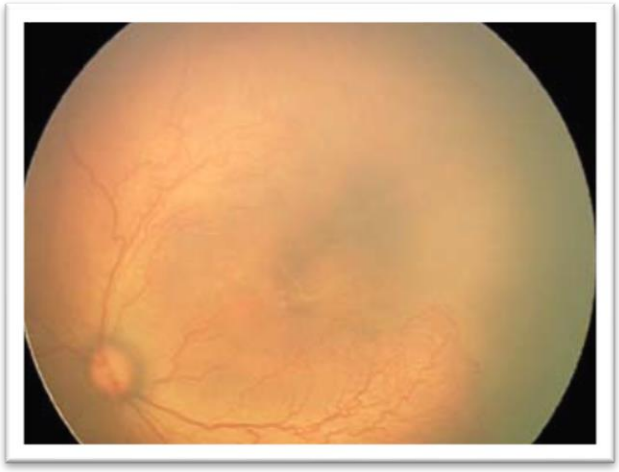


Figure 11: APROP

DIAGNOSIS

Screening criteria

Different countries have different criteria for screening. It has been found that the risk factors vary by a few numbers like the GA at birth, BW, and also due to increase in morbidity in developing and developed countries.

This individualization in different countries has been based on incidence studies conducted in the country.

There have been many studies of incidence in India lately. Infants selected for ROP screening differs on occurrence of ROP at various GA.

Centered on the existing frequency and risk factors that have been stated in various studies across India, screening should be carried out for infants with either of the following:

1. Birth weight < 2000 gm
2. Gestational age at birth < 34 weeks
3. Gestational age at birth between 34–36 weeks but having risk factors like
   i. Cardio-respiratory assistance / support
   ii. Extended Oxygen therapy
   iii. Respiratory distress syndrome
   iv. Chronic lung disease
   v. Fetal haemorrhage

vi. Transfusion of blood products

vii. Neonatal sepsis

viii. Exchange transfusion

ix. Intraventricular haemorrhage

x. Apnoeas

xi. Poor postpartum weight gain

4. Infants having an uneven clinical progression and are at a high risk, as defined by neonatologist or by a paediatrician.

Screening

Screening window:

Progression of ROP follows a distinct timeline as per Post Menstrual Age (PMA) rather than Post Natal Age (PNA) of the infant.

In Indian context, ROP may be detected even before 32 weeks of PMA. The median age at detection of Stage 1 ROP is 34 weeks. Threshold ROP appears at 34 – 38 weeks.

Complete retinal vascularization is seen by 40 weeks of GA.

Initial examination:

All the neonates who require screening should receive their first screening at 4 weeks of birth. Those infants with GA at birth < 28 weeks or BW < 1200 grams should receive their first screening at 2-3 weeks after delivery.

Follow up:

Table 2: Follow up interval for ROP Screening

Zone of retinal findings	Stage	Follow up interval
Zone 1	Immature vasculature	1-2 weeks
	Stage 1 or 2	1 week or less
	Regressing ROP	1 – 2 weeks
Zone 2	Immature vasculature	2 – 3 weeks
	Stage 1	2 weeks
	Stage 2	1 – 2 weeks
	Stage 3	1 week or less
	Regressing ROP	1 – 2 weeks
Zone 3	Stage 1 or 2	2 – 3 weeks
	Regressing ROP	2– 3 weeks

Further examinations can be stopped when:

- There is Zone III retinal vascularization without prior Zone I / II ROP
- There is complete retinal vascularization.
- PMA of 45 weeks and no pre-threshold disease or worse ROP is present
- There is regression of ROP.

Preparation

Personnel:

1.Screening should be carried out by an expert ophthalmologist.

2.Attendance of a neonatologist/paediatrician and a nurse is also needed.

Place of examination:

- Screening should be carried out preferably in the Neonatal ICU itself, under the supervision of the attending paediatrician/neonatologist.
- Place should be warm and clean.
- If babies are being screened at the Ophthalmologist's office, basic resuscitation equipment must be present.
- Pulse-oximeter monitoring should be done for critically ill babies.

Equipment:

Following instruments are required for screening:

- Indirect ophthalmoscope (wireless is preferable)
- 20 D, 28 D lens
- Paediatric Alfonso speculum
- Infant scleral depressor
- Dilating eye drops
- Topical anaesthetic eye drops
- Topical antibiotic eye drops
- Sterile cotton and gloves
- Documentation sheet to record the findings

Dilating eye drops:

Any of these eye drops can be used:

- Combination of Phenylephrine (2.5 %) and Tropicamide (0.4 %) eye drops
- Tropicamide (0.5 %) eye drops
- Cyclopentolate (0.5 %) eye drops
- Phenylephrine (2.5%) eye drops + Tropicamide (0.5%) / Cyclopentolate (0.5%) eye drops

Tropicamide:

- It is an antimuscarinic drug that producing short-acting mydriasis when applied as eye drops.
- Due to short duration of action (4–8 hours), it is commonly used for dilated fundus examination.
- Dosage in new-born - 0.5%.

Cyclopentolate:

- It causes both mydriasis and cycloplegia and also acts as a muscarinic antagonist.
- Onset of action takes 30–60 minutes and action lasts for about 24 hours.
- Dosage in new-born - 0.5%.

Phenylephrine:

- Acts as an adjunct with Tropicamide or Cyclopentolate
- It can cause an increase in the BP.
- Dosage in new-born - 2.5%.

Screening Procedure

a) **Pupillary dilatation:**

- Pupils are dilated using dilating eye drops.
- One drop of Tropicamide 0.5% is instilled in both the eyes, once in 10-15 minutes. It is repeated 3 times. It is started 1 hour before the schedule for the examination.
- After this, one drop of Phenylephrine 2.5 % eye drops is instilled just before the examination.

b) **Anaesthetic eye drops:**

- Topical anaesthetic eye drops (commonly Proparacaine 0.5% eye drops) are instilled 10 minutes before the examination.

c) Minimizing risk to the baby

- The examination is done after the pupils are fully dilated.
- Following this, lid retractors are used, and scleral depression as needed.
- Baby should be monitored for possibility of arrhythmia, bradycardia, hypoventilation, apnoea, asystole or aspiration
- Hand washing and change of gloves is performed in between each examination.
- Sterile instruments are used for each examination.

d) Infant physiological monitoring

- In case of an infant who is severely ill, a pulse oximeter has to be connected
- At any time of the examination, if the infant develops severe bradycardia or is not maintaining oxygen saturation, the examination should be halted and the appropriate measures have to be taken to improve the condition of the infant.

e) Diagnostic eye examination

- The infant is well clothed, wrapped and should have received a feed and burped an hour before screening.
- Pupil should be dilated at least 30 minutes before the examination.
- Informed consent must be obtained from the parents.
- The infant is swaddled, arms restrained to minimize movements and an assistant positions the infant for the examination.
- Topical anaesthetic drop must be applied.
- Paediatric eye speculum should be applied 30 seconds after anaesthetic drop.
- The use of oral sucrose may be considered to help with analgesia.
- The lid speculum is inserted beneath the lid margins.

f) Examination procedure

- Anterior segment has to be examined with the condensing lens focusing on cornea, iris and lens to look for any media opacity, tunica vasculosa lentis, dilated iris vessels and extent of pupillary dilatation.
- Posterior segment examination is then done with indirect ophthalmoscope using 20D/28D lens.
- The posterior pole as well as the peripheral retina is examined.

- Sclera depression can be done with wire vectis or specially designed paediatrics depressor if required.
- The findings are then recorded according to the ICROP guidelines and the parents are instructed about the same with an emphasis to strictly adhere to follow up schedule.
- One drop of antibiotic drop eye drop is instilled in each eye at the completion of examination.
- Infant is then observed for 15 minutes before handing over to parents.

Step 1:

The examining ophthalmologist will examine the posterior pole, and determine the following:

i. If there is plus disease which is defined as two or more quadrants of vascular dilation and tortuosity using standard photographs of plus disease for reference.
ii. If plus disease is not present, the presence or absence of pre-plus disease using standard photographs of pre-plus disease for reference.

Step 2:

The examining ophthalmologist will then examine the remainder of the retina to determine and document the stage, zone and extent of ROP if present.

i. Scleral depression is used as needed to visualize the entire fundus out to the ora serrata.
ii. Attention is given to area of scleral indentation, but also adjacent to it to detect peripheral ROP that may be posterior to the downslope of the indentation.

iii. Each quadrant is examined, and the findings are recorded using the ICROP system in the Data Collection Form.

Recording the findings in the screening form:

Apart from the demographic data, GA, PMA, BW, the following are documented:

a) Zone of vascularization,

b) Stage of ROP

c) Extent of ROP (in clock hours)

d) Presence of plus, or pre-plus disease,

e) Presence of AP-ROP

f) Whether treatment is indicated

g) Follow-up date.

TELEOPHTHALMOLOGY BASED SCREENING MODELS[158]

With increasing burden of the disease and lack of specialists trained in vitreoretina capable of performing widespread screening, there is a need for innovative models using teleophthalmology, wherein a trained ophthalmic technician takes images of the retina of the infant and transmits it to a nodal centre where an ophthalmologist can interpret the images and the course of treatment can be advised.

Two such projects are in action, the ITCROPS[159] and KIDROP[160]

RETCAM

RetCam is a camera capable of taking colour fundus photographs of a wide-field of the retina in preterm infants. It can be used as substitute for indirect ophthalmoscopy in ROP screening. It is an established device for retinal imaging to date and has been used for ROP imaging for over two decades.

It is a portable camera and it can help in teleophthalmology by storing, transmitting the photos to an expert who can then review, analyze the photos and sequentially compared over time. Studies were done to compare the RetCam and the indirect ophthalmoscope, and they have shown a good specificity but a variable sensitivity.[161] It also has drawbacks like high cost and also when media is hazy, the image quality is poor, so it can not completely replace indirect ophthalmoscope in ROP screening.

Photograph 1: RETCAM

PICTOR

The PICTOR handheld camera has been studied most widely for the purpose of ROP screening.[162] It has a limited field of view (45°) and also difficult alignment issues which limit its use and reduced its popularity and wider adoption.

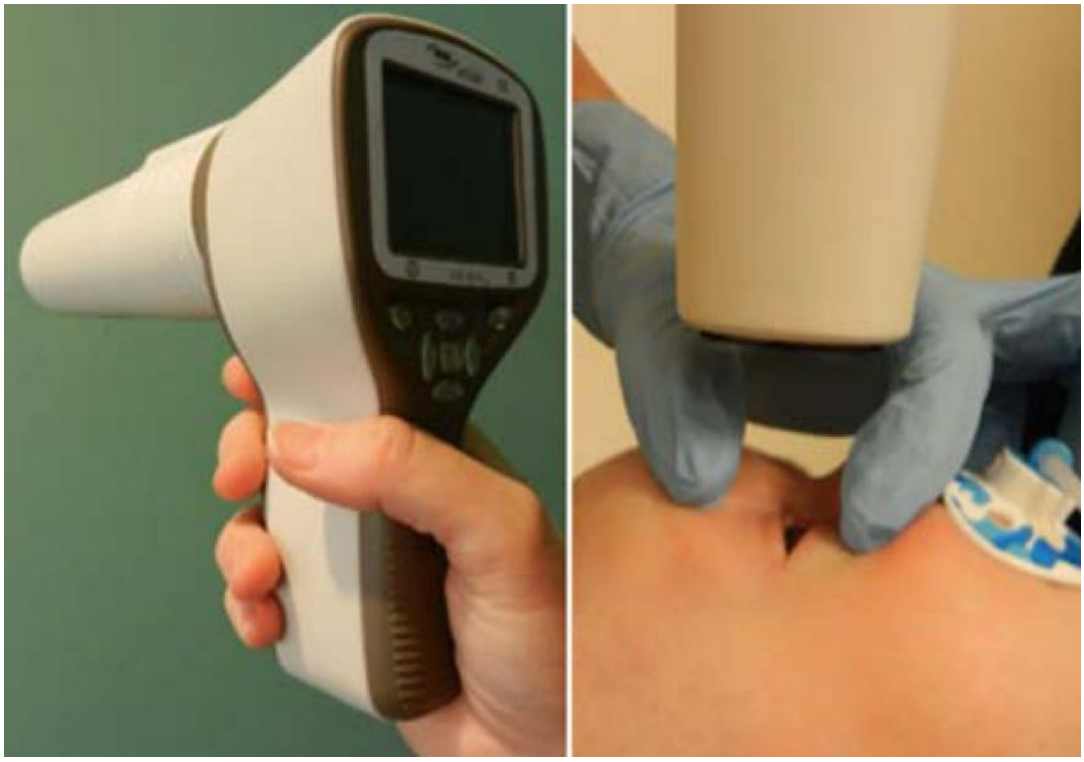


Figure 12: Pictor handheld camera

3NETRA NEO

This ultra-widefield retinal imaging camera has been very useful in teleophthalmology as it has been found to have higher sensitivity, specificity and a higher field of view compared to the other modalities. It is economical compared to the RETCAM and hence more affordable for most of the centres.

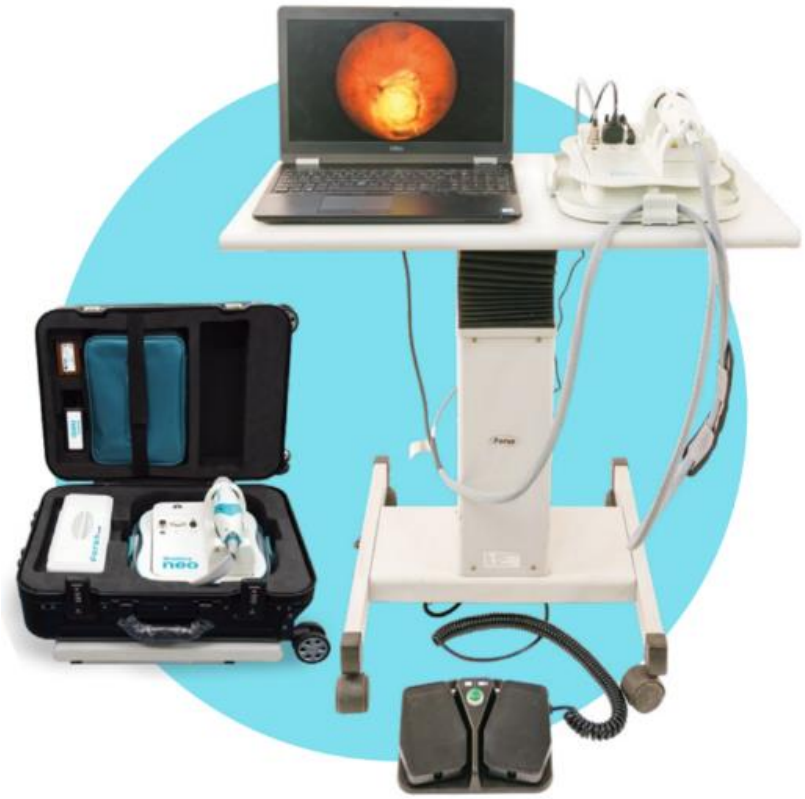


Figure13: 3netra NEO camera

Other available cameras for wide-field imaging of patients with ROP:

- ICON
- MII RetCam
- Optos
- 200-TX Optomap

TREATMENT

Aim of treatment:

1.To reduce the incidence of retinal detachment

2.To reduce the incidence of blindness.

The Early Treatment of Retinopathy of Prematurity (ETROP) trial concluded in the US stated that "Early treatment of high-risk pre-threshold ROP significantly reduced unfavourable outcomes to a clinically important degree."

They compared the outcomes of early treatment with laser to determine whether earlier treatment using ablation of the avascular retina in high-risk pre-threshold retinopathy of prematurity (ROP) results in improved grating visual acuity and retinal structural outcomes compared with conventional treatment.

In this study, they randomized about 416 infants who fit in their inclusion criteria of high – risk with pre-threshold disease and prone to develop unfavourable outcome into 2 categories, the conventional treatment and another as early treatment.

They used several parameters to assess the risk level in a programme like the degree of ROP, rate of its progression, BW, GA and also considered ethnicity.

They classified eyes as 'high-risk' in which there was 15% chance or 'low-risk' where there was a chance of <15% for unfavourable outcome if no treatment was given.

Their results showed that there was benefit in the early treatment group. Based on these results, 2 different types of ROP were advised:

Table 3: Types of ROP based on ETROP study

Type of ROP	**Zone**	**Stage**	**Plus disease**
Type 1	I	Any	With
	I	3	With/without
	II	2 or 3	With
Type 2	I	1 or 2	Without
	II	3	Without

In case of Type 1 ROP, peripheral retinal ablation is carried out and in case of type 2 ROP continuous monitoring of infant by screening was recommended.

TREATMENT MODALITIES

Retinal ablation of the peripheral avascular retina is accomplished either through cryoablation or by LASER ablation.

In the recent times, frequency doubled Nd: YAG LASER has almost totally replaced cryotherapy, due to its better post-op outcomes and lesser ocular and systemic complications. Also, the damage to adjacent tissues is less with LASER in comparison to cryotherapy. Other advantages include better visibility of areas being ablated, thereby decreasing the hazards of skipping the retinal area requiring ablation.

Another advantage is its portability. The laser equipment can also be used in the NICU itself. Also, unlike cryotherapy, LASER can be performed under local anaesthesia, topical anaesthesia, under sedation or under general anaesthesia, depending on the availability of resources and expertise. Ablation for ROP should be done for the entire avascular retina from the ridge to the ora serrata, with burn space of 0.5 to 1 burn-widths.

CRYOTHERAPY

Cryotherapy is an ablative procedure, previously used in Type 1 ROP. Its aim is to destroy the avascular peripheral retina so as to stop the rapidly growing vessels, which presumably are being driven to grow by the angiogenic factors being released by the peripheral avascular retina.

The Cryo-ROP study[108] is a milestone in the fight alongside ROP. The study recommended "cryoablation in cases where there is threshold ROP, which was described as zone I and zone II disease with 5 contiguous or 8 aggregate clock-hours of ROP in stage 3 with plus disease."

Technique:

Cryo probe is used for creating contiguous cryo marks at the avascular retina. Is has to be done under continuous vitals monitoring. General anaesthesia is the preferred mode of sedation. Cryotherapy is delivered using a cryotherapy probe, preferably the paediatric probe that is in the shape of a hammerhead. Under direct observation, cryotherapy to the fundus is delivered continuously to avoid over or re-treatment. After the cryo treatment, the infant has to be discharged under the cover of topical steroid, cycloplegic and antibiotic eye drops.

LASER PHOTOCOAGULATION

It has been established as the gold standard treatment for retinal ablation in the recent times. We use a Laser mounted onto the indirect ophthalmoscope to deliver the energy to the fundus of the eye.

McNamara *et al*., in their study, concluded that "laser therapy is as effective as cryotherapy in the treatment of ROP."[163] The study also showed that infants who had undergone LASER photocoagulation had lesser ocular and systemic complications. During Laser, topical anaesthesia was usually preferred. ETROP stated benefits in the early treatment group especially in presence of plus disease in any zone and vitreous haze.

In the recent times, use of TSDL has also been assessed in threshold ROP cases for treatment. The results suggested that "It is efficient in the treating infants with threshold ROP just like diode laser used via transpupillary route. TSDL was found to be more advantageous in preventing cataract formation." Studies have also concluded, "TSDL to an alternative to cryotherapy for treatment of ROP."[164]

Infant preparation:

The mother should be asked to stop feeds to the infant at least 3 hours before to prevent aspiration. Infant is then started on intravenous fluids and continuously being monitored for vitals and saturation. Full dilatation of pupil is obtained with dilating eye drops.

Anaesthesia:

Depending on the expertise of the surgeon, topical anaesthesia/sub tenon / general anaesthesia/iv sedation. Additionally, sedation/analgesia is needed which can be arranged by using sucrose dips. The LASER can also be performed in the NICU if conditions are not permitting for shifting infant to Operation theatre.

Procedure:

LASER is given to both the eyes usually in the same sitting, except when the infant is unstable or if there is any other contraindication. If the infant fails to tolerate the procedure, the procedure has to be abandoned and taken up later. Vitals and oxygen saturation are very closely monitored.

Post-operative monitoring:

Immediately post laser, in critically ill infants, they should be monitored in the NICU till their condition improves. In other cases, the infant can be handed over to the parent immediately and feeds started after 30 minutes.

Monitoring after LASER therapy:

Post laser, initial examination is done 5 – 7 days later. Monitoring should be continued at least every week till signs of regression and decreasing disease activity is seen.

Tropicamide 0.5% eye drops should be instilled 2 times a day.

Antibiotic eye drops should be instilled 3 times a day.

ANTI-VEGF AGENTS

VEGF has been found to be an important mediator for abnormal retinal vasculogenesis as seen in ROP. It was used initially to target neovascularization in ARMD and likewise, it is useful for treatment of proliferative retinopathy. In cases of ROP, use of anti- VEGF in Phase 2 [165] has been found to be effective.

The use of anti- VEGF in ROP started in the BEAT-ROP study[166], where in the effect of intravitreal Bevacizumab was compared with that of laser therapy. It was found that monotherapy with Intravitreal bevacizumab was having benefit over laser in Zone I disease. Few studies have shown that it can also reduce refractive errors in childhood.[167] They are also not usually recommended due to their systemic effects. A report by Bazvand *et al*.,[168] reported: "Hypertension and ischemic stroke one week after they injected Aflibercept." Ranibizumab has a shorter half-life, so lesser systemic side effects compared to Bevacizumab. Due to shorter half-life, it is more prone to develop ROP again. Hence, the infant is more closely monitored when Ranibizumab is administered.[169] RAINBOW trial showed Ranibizumab to have better outcomes than laser.[170]

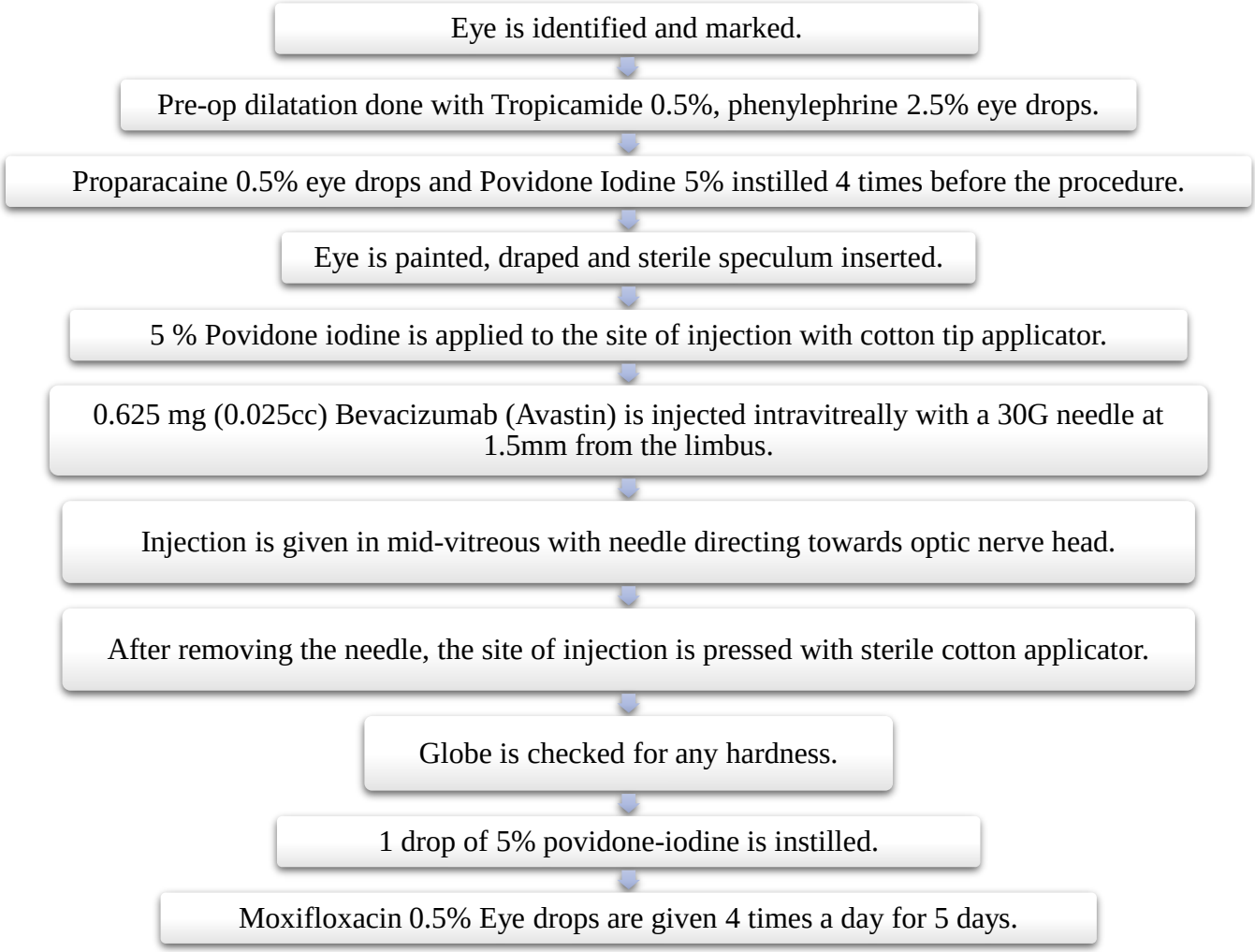
It is given only to those infants with:

1. APROP
2. In selected cases of Type, I ROP in posterior zone II where laser treatment would be inadequate.

Procedure:

The parents should be informed about the experimental nature of the treatment and possible complications are explained and informed consent is taken.

Flowchart 2: Procedure for Intravitreal injection of anti- VEGF agents



Follow up:

It is done next day, 1 week later, then every 1 – 3 weeks, depending on the regression of ROP. If recurrence of ROP occurs, then Laser is offered.

METHODOLOGY

METHODOLOGY

The present study was conducted at the Department of Ophthalmology and the Department of Paediatrics and Neonatology, KLES Dr. Prabhakar Kore Hospital & Medical Research Centre, Belagavi from 1st January 2019 to 31st December 2019 to assess the incidence, risk factors and treatment outcomes of Type 1 ROP in infants admitted to the NICUs of KLES Hospital.

METHOD OF DATA COLLECTION

STUDY POPULATION:

All the preterm infants screened at the NICUs of KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi and being referred to the KLE Ophthalmology Department for evaluation with inclusion criteria of this study.

SOURCE OF DATA

A data collection instrument was used in which the data was collected from:

1. By interviewing the parents
2. Hospital records
3. Examination of the infant

STUDY DESIGN

A prospective, non-comparative, longitudinal study with a short follow up.

STUDY PERIOD

One year from 1st January 2019 to 31st December 2019

SAMPLE SIZE

The sample size was calculated according to the formula:

$$n = \frac{z_\alpha^2 P(1-P)}{d^2}$$

P : Percentage of prevalence

P = 35.8%

d : Percentage likely difference in the prevalence.

d = 10 %

z_α : Level of significance.

For 1% level of the significance Zα = 2.576.

Sample size calculated by substituting these variables comes to 153.

Therefore, the minimum number of subjects to be enrolled = 153

SELECTION CRITERIA

Inclusion criteria:

1. Infants born with birth weight ≤ 2000 gm
2. Infants born at a gestational age ≤ 34 weeks
3. Infants born at a GA from 34 to 36 weeks and with risk factors:
    a. Need for Cardio-respiratory support
    b. Prolonged (> 7 days) oxygen therapy
    c. RDS
    d. Chronic lung disease
    e. Fetal haemorrhage
    f. Transfusion of blood products
    g. Neonatal sepsis
    h. Exchange transfusion
    i. Intraventricular Hemorrhage
    j. Apneas
    k. Poor post-natal weight gain.
4. Those infants who have been determined by the Neonatologist / Paediatrician as having an unstable clinical course.

Exclusion criteria:

1. Those infants whose parents have refused to consent for the study.
2. Infants who expired before full vascularization of the retina.
3. Failure to follow up due to other reasons.

CONSENT AND ETHICAL CLEARANCE

Informed/ written consent of parents was taken after explaining in detail about the methods and procedures involved in the study in their own vernacular language. Ethical clearance was obtained.

DEFINITION OF RISK FACTORS

Apnoea:

It is defined as a cessation of respiration for > 20 sec, which required resuscitation with bag and mask/ with 100% O_2.

Sepsis:

It was diagnosed by clinical picture, changes in leukocyte count, elevated CRP (C-reactive protein) and positive blood culture.

Respiratory Distress Syndrome (RDS):

Presence of at least two of the following criteria:

- Respiratory rate > 60/min in a quiet and resting baby.
- Sub costal/ intercostals space recessions.
- Expiratory grunt.

Preparation of the child

a) Pupillary dilatation:

Pupils were dilated using a mixture of Tropicamide 0.5% and Phenylephrine 2.5% eye drops. The eye drops were instilled one drop in both the eyes, once in 10-15 minutes. They were instilled 4 times and were started 1 hour before the scheduled time for the examination. After these, a drop of Phenylephrine 2.5 % eye drops is instilled just before the examination.

b) Anaesthetic eye drops:

Topical anaesthetic eye drops (commonly Proparacaine 0.5% eye drops) were instilled 10 minutes before the examination.

c) Infant care:

Care was taken to see that the infant was not fed till 30 min before examination as. Any resistance in dilatation was duly noted. To prevent absorption through skin, any eye drops that came out of eyes to cheeks were wiped off with sterile cotton.

d) **Infant physiological monitoring** was done during examination of sick infants using a pulse oximeter.

Instruments used:

a) Cordless Binocular Indirect ophthalmoscope

b) 20 D and 28 D lens.

c) Infantile Alfonso wire speculum.

d) Scleral depressor.

Schedule of the first examination:

The following table was used to schedule the first examination

Table 4: Timing of first screening eye examination based on gestational age at birth and birth weight.

GA at birth examination	**Chronological age**
< 28 weeks	2 weeks
≥ 28 weeks	4 weeks
Birth weight	**Chronological age**
< 1200 grams	2 weeks
≥ 1200 grams	4 weeks

Procedure:

All the infants who met at least one of the inclusion criteria were included in the study.

The infants were enrolled into the study at birth. Parents were explained about the need for examination, nature of the examination and informed consent was taken. Demographic history, prenatal and post-natal risk factors were recorded using a data collection instrument.

The first examination was performed in a temperature-controlled room or at the Neonatal ICU, in the existence of a neonatologist.

Indirect ophthalmoscopy was done. Initially without, then with an infantile Alfonso speculum for separating the eyelids.

The room illumination was kept minimum. Initially, we examined the anterior segment, to look for pupillary dilatation, tunica vasculosa lentis, iris neovascularization, and clarity of the lens and media. Then the fundus of the eye was examined.

Fundus examination:

Step 1: First the posterior pole was examined to look for

1) Evidence of Plus disease.
2) If plus disease was absent, then the presence or absence of pre-plus disease using standard photographs for reference.

Step 2: Then the remainder of the retina was examined to look for and to document the zone, stage and extent of ROP if present.

1) Scleral depression was used as needed to visualize the entire fundus out to the ora serrata.
2) Each quadrant was examined, and the findings recorded using the ICROP system.

Method of statistical analysis:

The following methods of statistical analysis have been used in this study.

1.The results for each parameter (numbers and percentages) for discrete data and average (mean ± Standard deviation) for continuous variables are presented in Tables and Figures. Chi-square was used to check the association between categorical variables.

Table 5: Chi-Square ($\chi 2$) test for (2 x 2 tables)

GROUP	Attribute Characteristic finding		
	ABSENT	PRESENT	TOTAL
Group 1	a	b	a+b
Group 2	c	d	c+d
Total	a+c	b+d	N

a, b, c, d are the observed numbers.

$$\chi 2 \text{ with 1 DF} = \frac{N(ad-bc)^2}{(a+b)(c+d)(a+c)(b+d)}$$

N is the Grand Total

Degrees of Freedom (DF): Number of observations that are free to vary after certain restrictions have been placed on the data.

DF = (r-1)×(c-1) where [r = rows; c=columns]

2. Student 't' test:

The student 't' test was used to determine whether there was a statistical difference between male and female subjects in the parameters measured.

Student's t-test is as follows:

$$t = \frac{\overline{x}_1 - \overline{x}_2}{\sqrt{(s^2(\frac{1}{n_1} + \frac{1}{n_2}))}}$$

t	=	t-value
x_1 and x_2	=	means of the two groups being compared,
s_2	=	pooled standard error of the two groups,
n_1 and n_2	=	number of observations in each of the groups.

The association between potentially related risk factors with type 1 ROP and without type 1 ROP were studied initially through a univariate analysis.

The categorical variables were assessed using Pearson chi-square and Yates correction applied where needed.

Odds Ratio (OR) and 95% confidence interval (CI) was calculated.

To estimate the independent effect of the factors that were significantly associated with Type 1 ROP and without Type 1 ROP the confounding effect they may have on each other, logistic regression analysis was done.

The variables were included if their respective univariate analysis yielded P<0.10.

A backward stepwise elimination procedure based on the likelihood statistics (using removal probability of 0.10 and considering the change in classification accuracy) was also performed to identify the best subset of variables.

In the whole analysis, the "*p*" value of less than 0.05 was taken as showing statistical significance.

Statistical Package for Social Science (SPSS - 20) was used for data analysis.

OBSERVATION AND RESULTS

OBSERVATION AND RESULTS

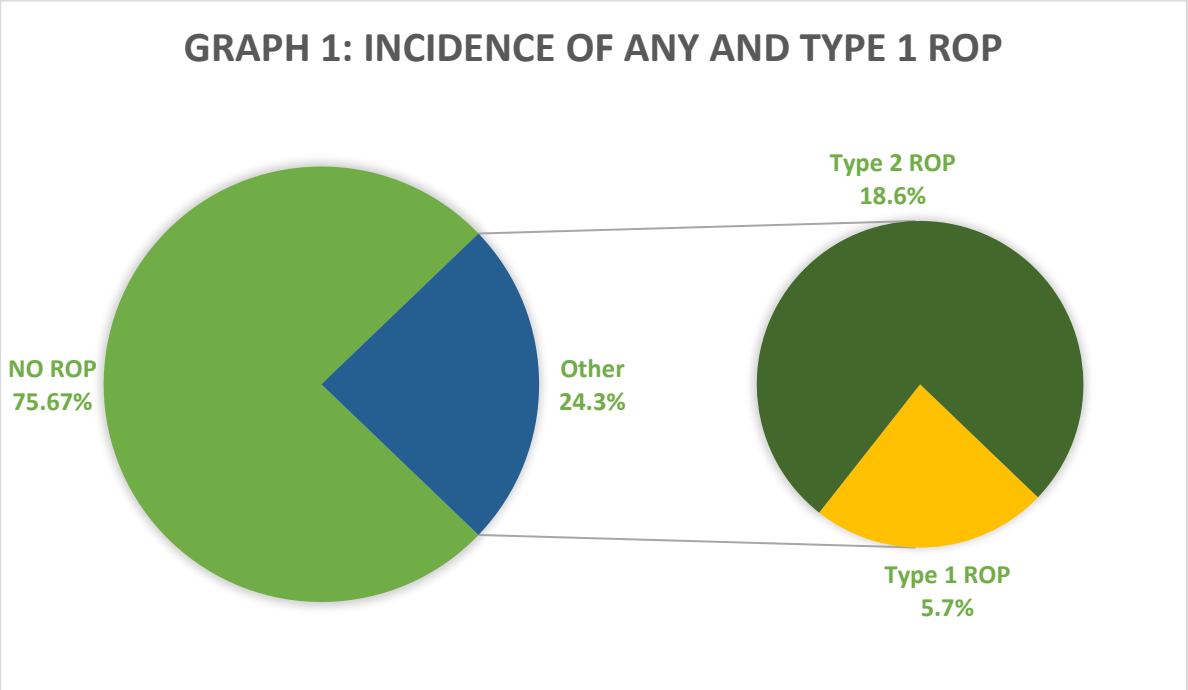
In our study, 526 eyes of 263 babies were included.

INCIDENCE

The incidence of **any ROP** was **24.3 %** and of **Type 1 ROP** in this study is **5.7%**

Table 6: Incidence of Type 1 ROP

TYPE 1 ROP	NUMBER	%
Present	15	5.7
Absent	248	94.3
Total	263	100

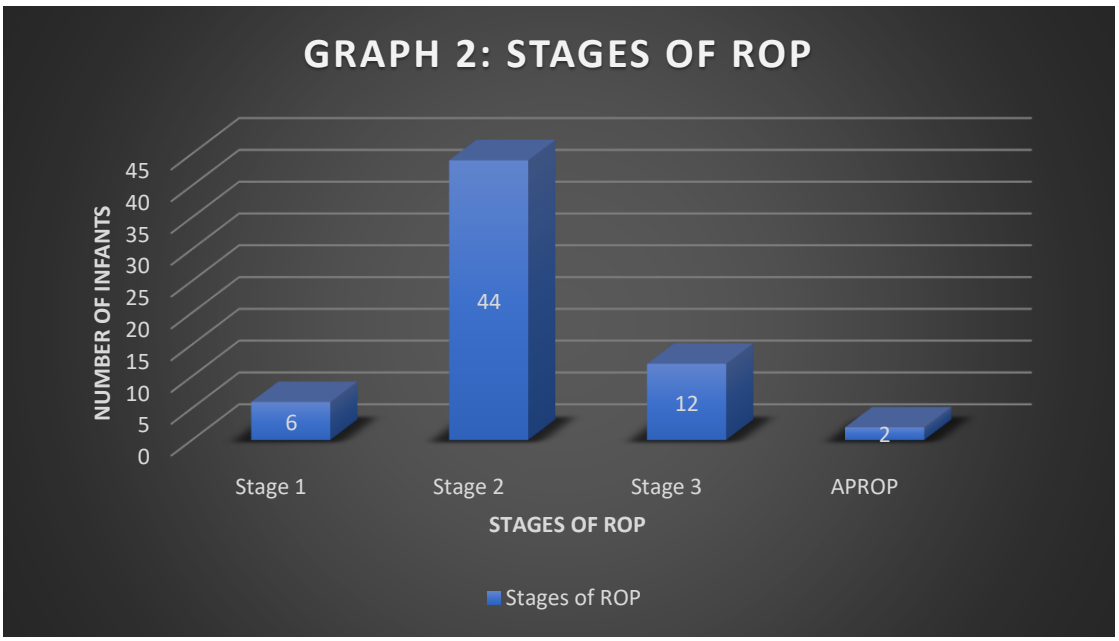


STAGES OF ROP

In this study, 6 infants had Stage 1 ROP, 44 infants had Stage 2 ROP, 12 infants developed Stage 3 ROP and 2 infants developed APROP.

Table 7: Stages of ROP

	RETINOPATHY OF PREMATURITY STAGES				
	1	**2**	**3**	**APROP**	**TOTAL**
ROP PRESENT	6	44	12	2	64
%	9.37	68.75	18.75	3.12	100%



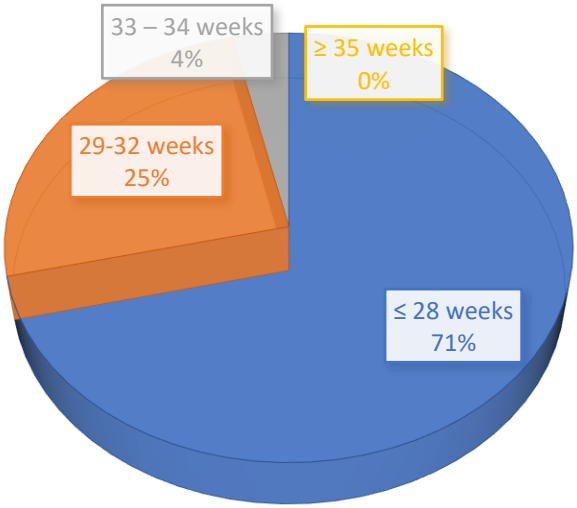
GESTATIONAL AGE AT BIRTH

Out of the 263 infants screened, 19 infants were born at GA < 28 weeks, 97 infants with GA between 29 – 32 weeks, 77 infants between 33 – 34 weeks and 70 infants at GA ≥ 35 weeks. Of these, 5 of the 19 infants born at GA < 28 weeks, 9 of 97 infants born with GA between 29 – 32 weeks, 1 of 77 infants born at GA between 33-34 weeks and none of the 70 infants born at GA ≥ 35 weeks developed Type 1 ROP.

Table 8: Gestational age at birth

GA AT BIRTH	TYPE 1 ROP	TOTAL	%	χ^2	p- value
≤ 28 weeks	5	19	26.32	24.3270	0.0001*
29-32 weeks	9	97	9.28		
33 – 34 weeks	1	77	1.30		
≥ 35 weeks	0	70	0.00		

GRAPH 3: GESTATIONAL AGE AT BIRTH AND TYPE 1 ROP

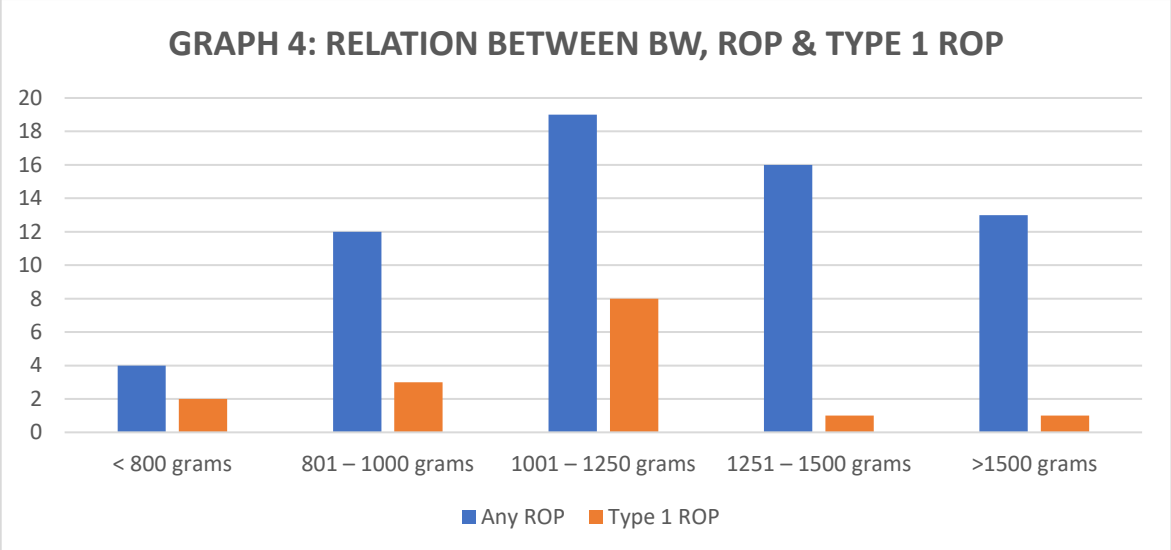


BIRTH WEIGHT

In this study, 2 of the 5 infants with BW < 800 gms, 3 of 19 infants with BW 801 – 1000 gms, 8 of 36 infants with BW 1001-1250 gms, 1 of 63 infants with BW 1251 -1500 gms, and 1 of 140 infants with BW > 1500 gms developed Type 1 ROP. BW was observed to be a substantial risk factor for the development of Type 1 ROP.

Table 9: Relation between BW and any ROP and BW and Type 1 ROP

Birth weight	Type 1 ROP	Total	%	χ^2	p- value
< 800 grams	2	5	40.00	41.2590	0.0001*
801 – 1000 grams	3	19	15.79		
1001 – 1250 grams	8	36	22.22		
1251 – 1500 grams	1	63	1.59		
>1500 grams	1	140	0.71		

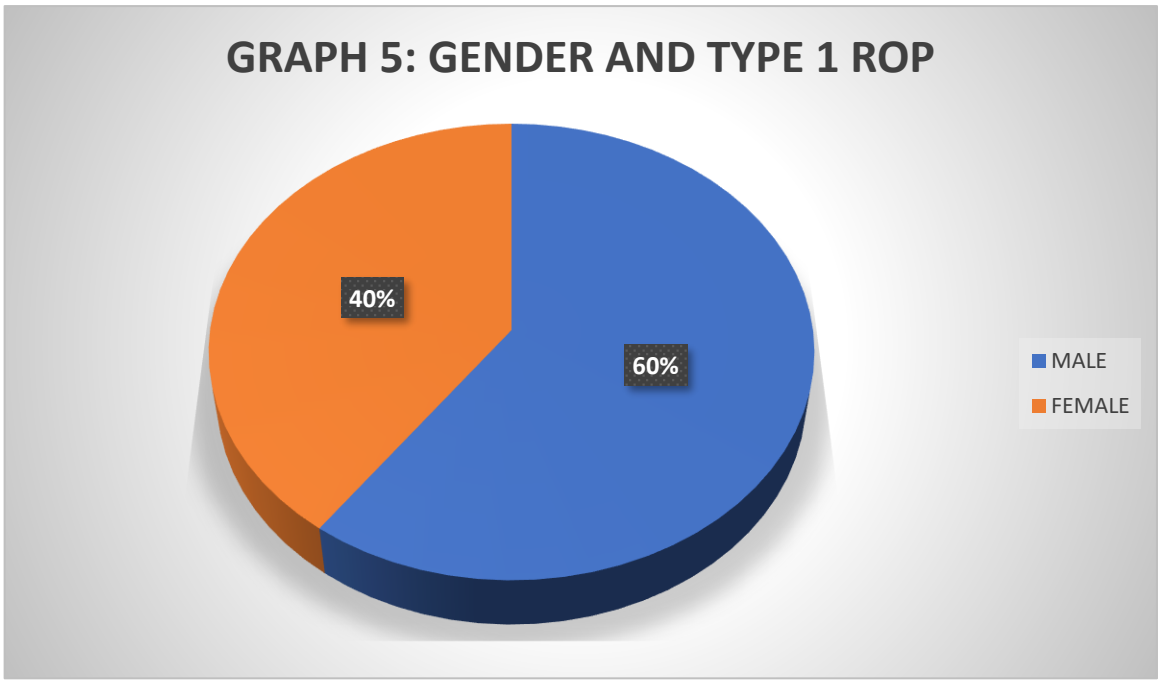


GENDER DISTRIBUTION

In this study, Type 1 ROP was seen 60 % in Males and 40 % in Females. It was not found to be statistically significant factor for the development of Type 1 ROP.

Table 10: Gender and Type 1 ROP

Type 1 ROP	Male	Female	Total
Present	9	6	15
Absent	146	102	248
Total	155	108	263



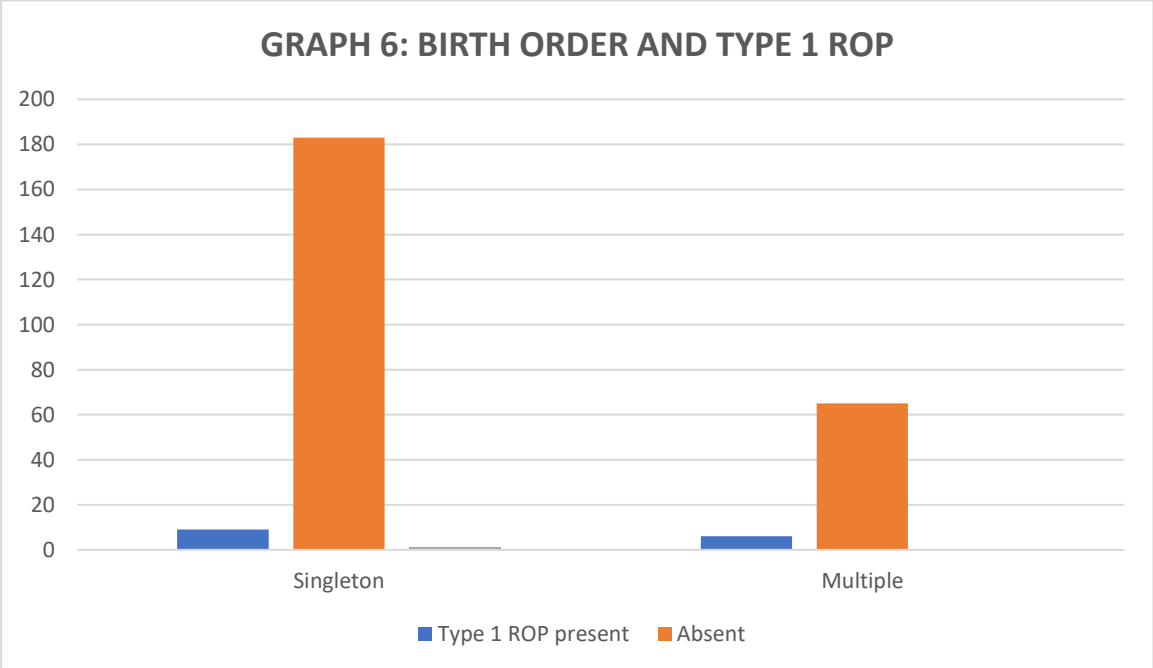
MATERNAL RISK FACTORS

BIRTH ORDER

In this study, Type 1 ROP was seen in 60 % of singleton pregnancies and in and 40 %multiple pregnancies. It was not a significant risk factor (p = 0.2430)

Table 11: Birth order and Type 1 ROP

Type 1 ROP	Singleton	Multiple	Total
Present	9 (4.69%)	6 (8.45%)	15
Absent	183 (95.31%)	65 (91.55)	248
Total	192 (73%)	71 (27%)	263

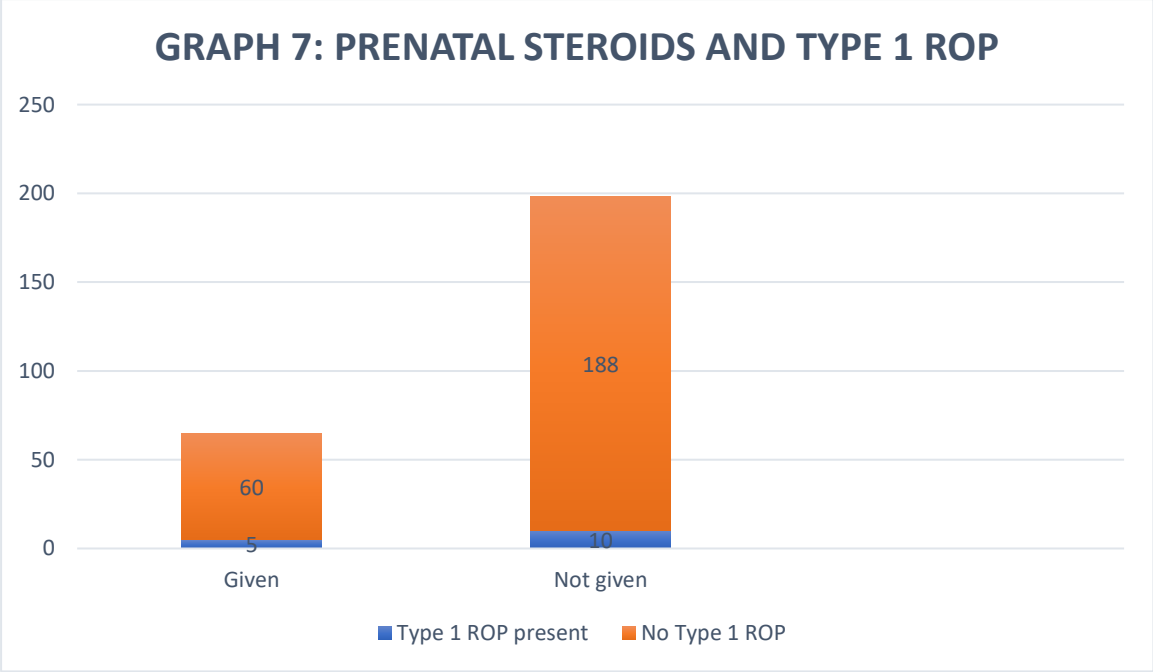


PRENATAL STEROIDS

Out of 263 infants screened, 65 infants were given prenatal steroids and 5 developed Type 1 ROP. Prenatal steroid administration was a significant risk factor for preventing Type 1 ROP. (p=0.4900) Yates correction 2.4190

Table 12: Prenatal steroids and Type 1 ROP

TYPE 1 ROP	Administered	Not administered	Total
Present	5 (7.69%)	10 (5.05%)	15
Absent	60 (92.30%)	188 (94.95%)	248
Total	65	198	263

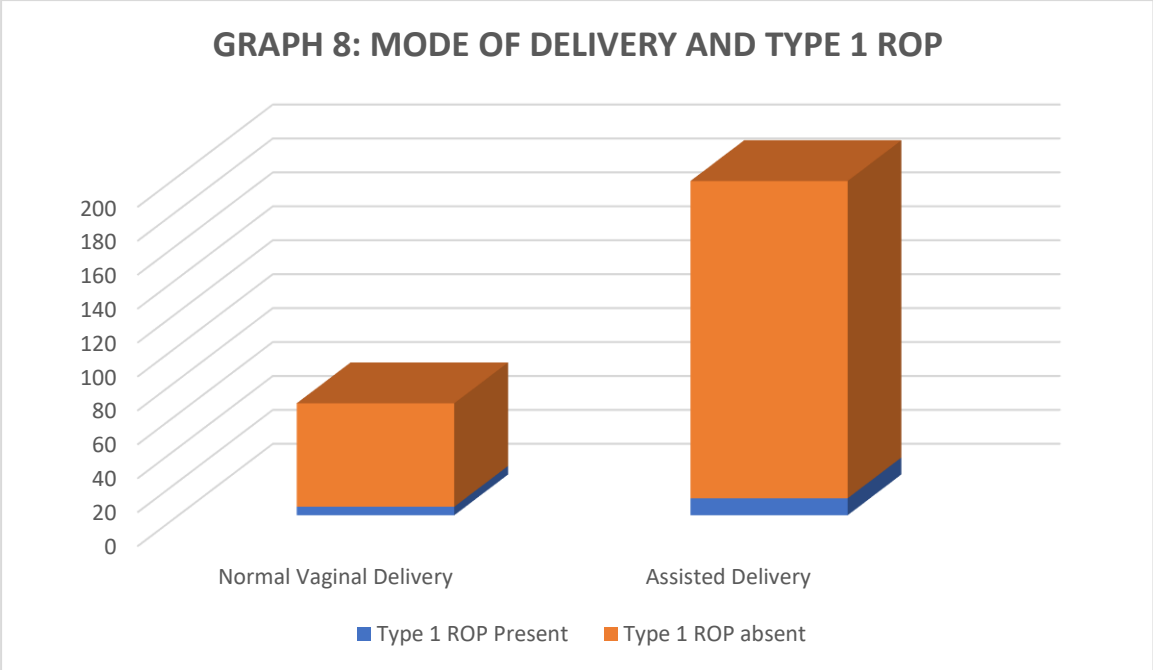


MODE OF DELIVERY

In this study, 197 infants were delivered by Assisted delivery i.e., by Lower Segment Caesarian Section & by Vacuum-assisted delivery (LSCS+V) and 66 were delivered by Normal Vaginal Delivery (NVD). The incidence was more in cases of Normal vaginal delivery. Mode of delivery was not found to be a substantial factor for the progression to Type 1 ROP.

Table13: Mode of delivery and Type 1 ROP

Type 1 ROP	NVD	LSCS + V	Total
Present	5 (7.58%)	10 (5.08%)	15
Absent	61 (92.42%)	187 (94.92%)	248
Total	66 (25.10%)	197 (74.90%)	263

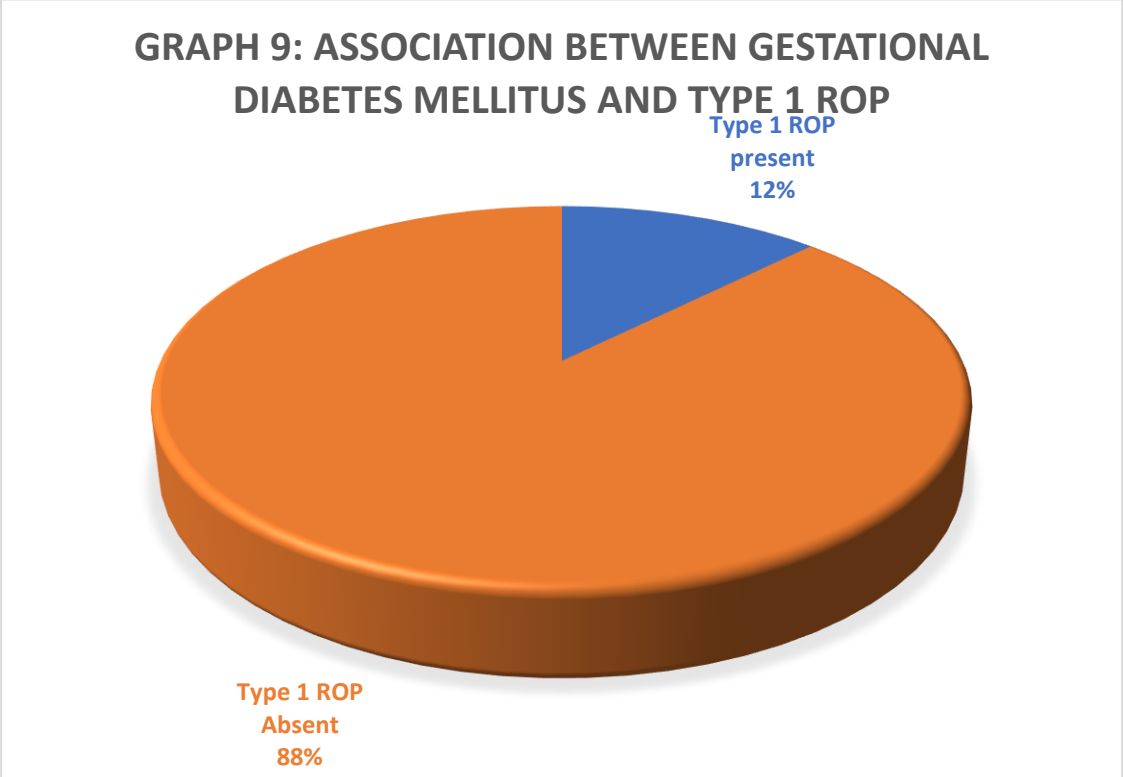


GESTATIONAL DIABETES

Out of the 263 infants included in this study, 24 were born to mothers having Gestational Diabetes Mellitus (GDM). Type 1 ROP was seen in 3 of these 24 infants. With a p-value of 0.1320, it was observed to be a non-substantial factor by univariate analysis for development of Type 1 ROP. (p=0.1320)

Table 14: Association of GDM with Type 1 ROP

Type 1 ROP	GDM Present	GDM Absent	Total
Present	3(12.50%)	12(5.02%)	15
Absent	21(87.50%)	227(94.98%)	248
Total	24	239	263

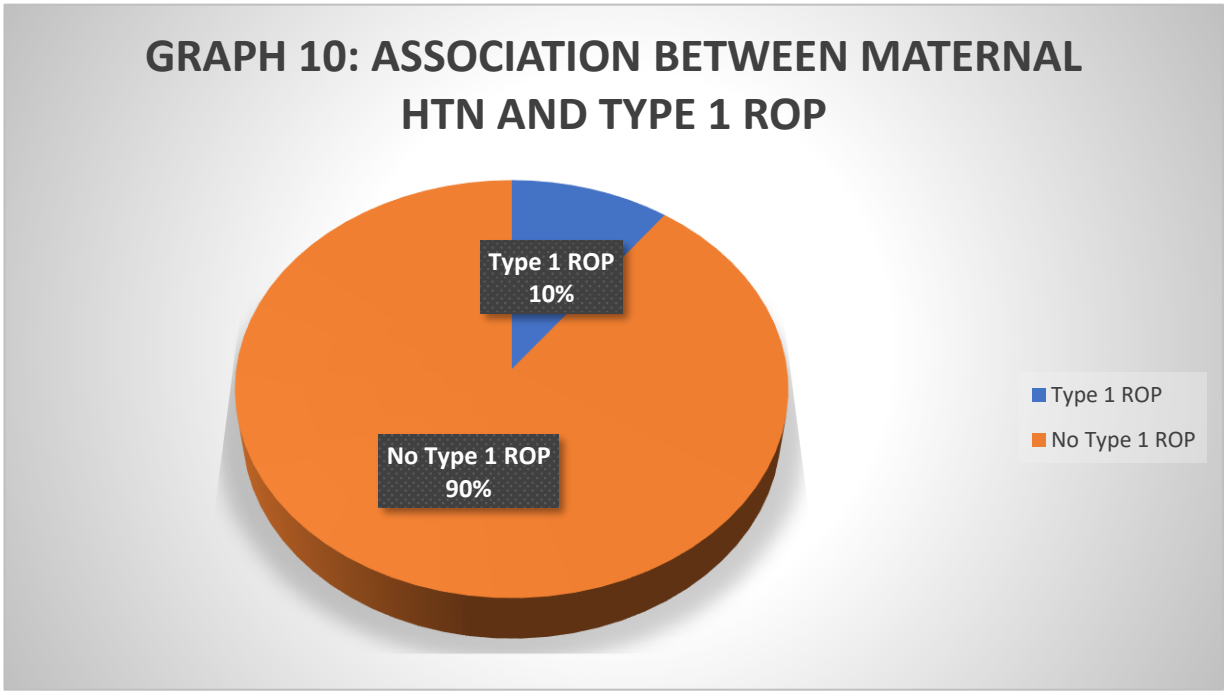


GESTATIONAL HYPERTENSION

Out of the 263 infants included in this study, 98 were born to mothers having Maternal Hypertension. Type 1 ROP was seen in 10 of 98 infants. With a p-value of 0.0150, it was found to be a substantial risk factor by univariate analysis for developing Type 1 ROP. (p=0.0150; $\chi^2 = 5.8830$)

Table 15: Association of Maternal HTN with Type 1 ROP

Type 1 ROP	Maternal HTN Present	Maternal HTN Absent	Total
Present	10 (10.20%)	5(3.03%)	15
Absent	88(89.80%)	160(96.97%)	248
Total	98	165	263

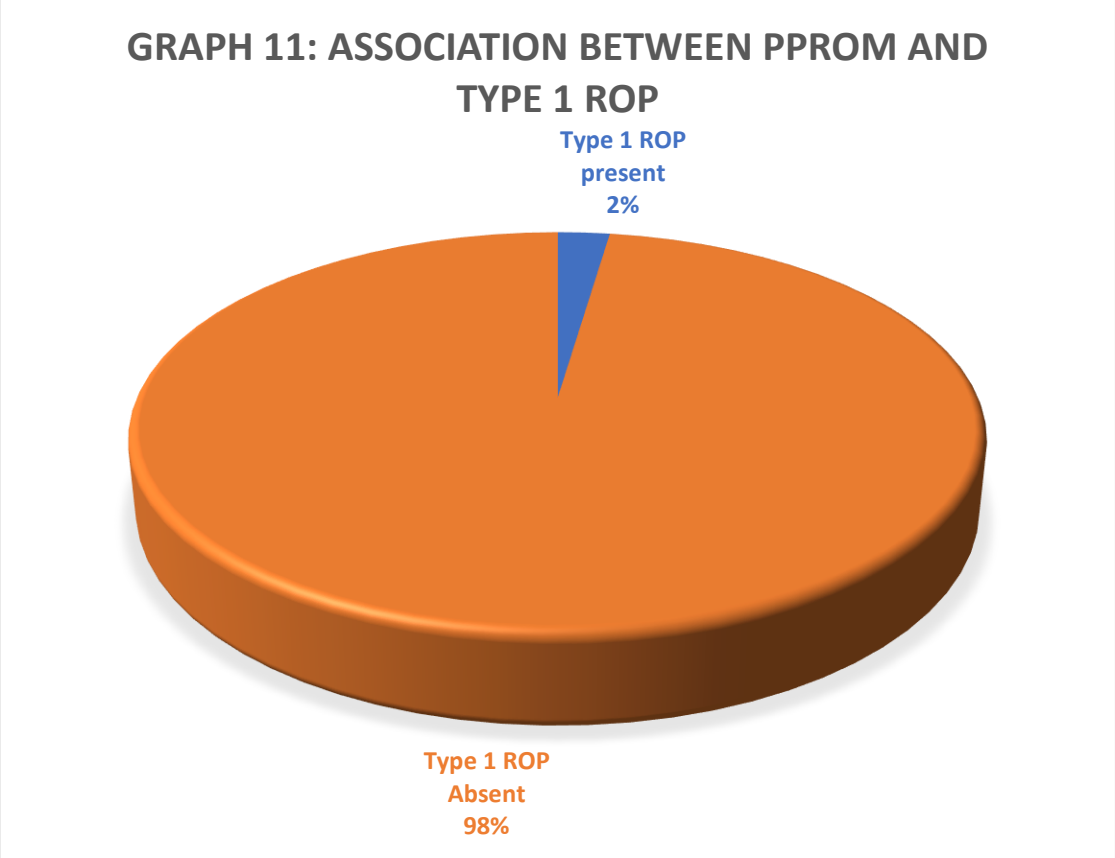


PPROM

Of the 263 infants, 15 were born to mothers who had PPROM. Of these, one infant developed Type 1 ROP. By univariate analysis, no significant association was found between PPROM and Type 1 ROP. (p=0.2960)

Table 16: Association of PPROM and Type 1 ROP

Type 1 ROP	PPROM Present	PPROM Absent	Total
Present	1 (2.33%)	14 (6.36%)	15
Absent	42 (97.67%)	206 (93.64%)	248
Total	43 (83.65%)	220 (16.35%)	263



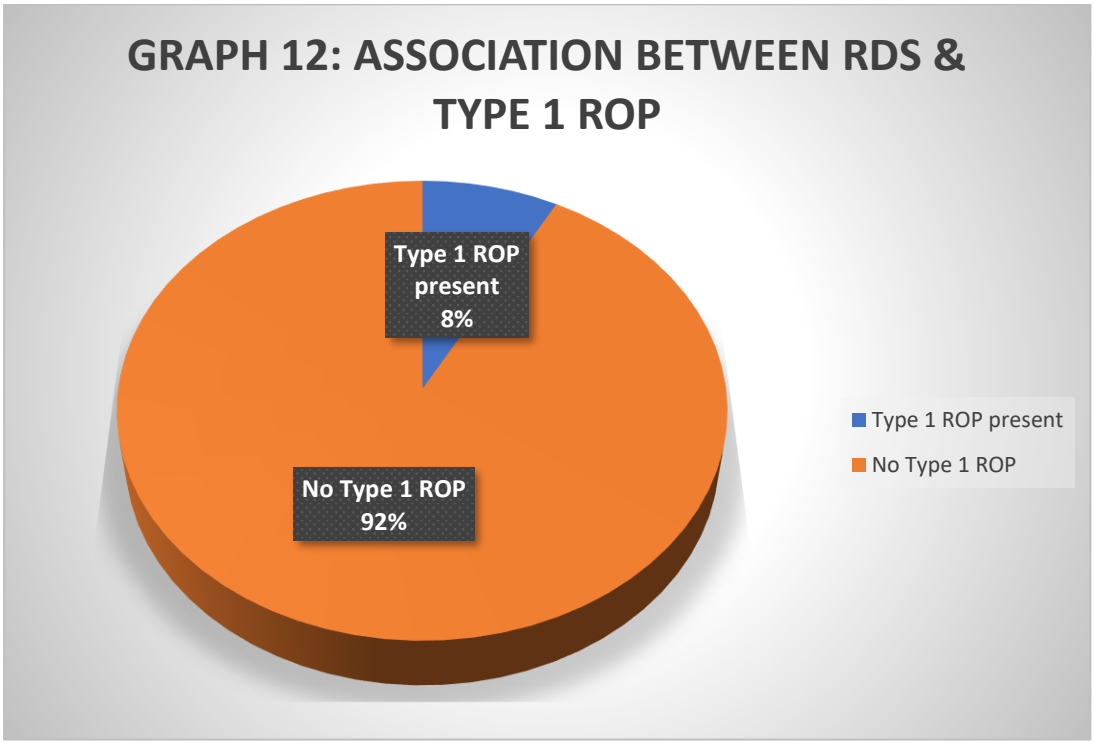
NEONATAL RISK FACTORS

RESPIRATORY DISTRESS SYNDROME

126 of the 263 infants included in this study had RDS. 10 of these 126 developed Type 1 ROP. By Univariate analysis, it was not found to be having any significant association with the development of Type 1 ROP. (p-value = 0.1340; $\chi^2 = 2.2430$)

Table 17: Association of RDS and Type 1 ROP

Type 1 ROP	RDS Present	RDS Absent	Total
Present	10(7.94%)	5(3.65%)	15
Absent	116(92.06%)	132(96.35%)	248
Total	126(47.91%)	137(52.09%)	263

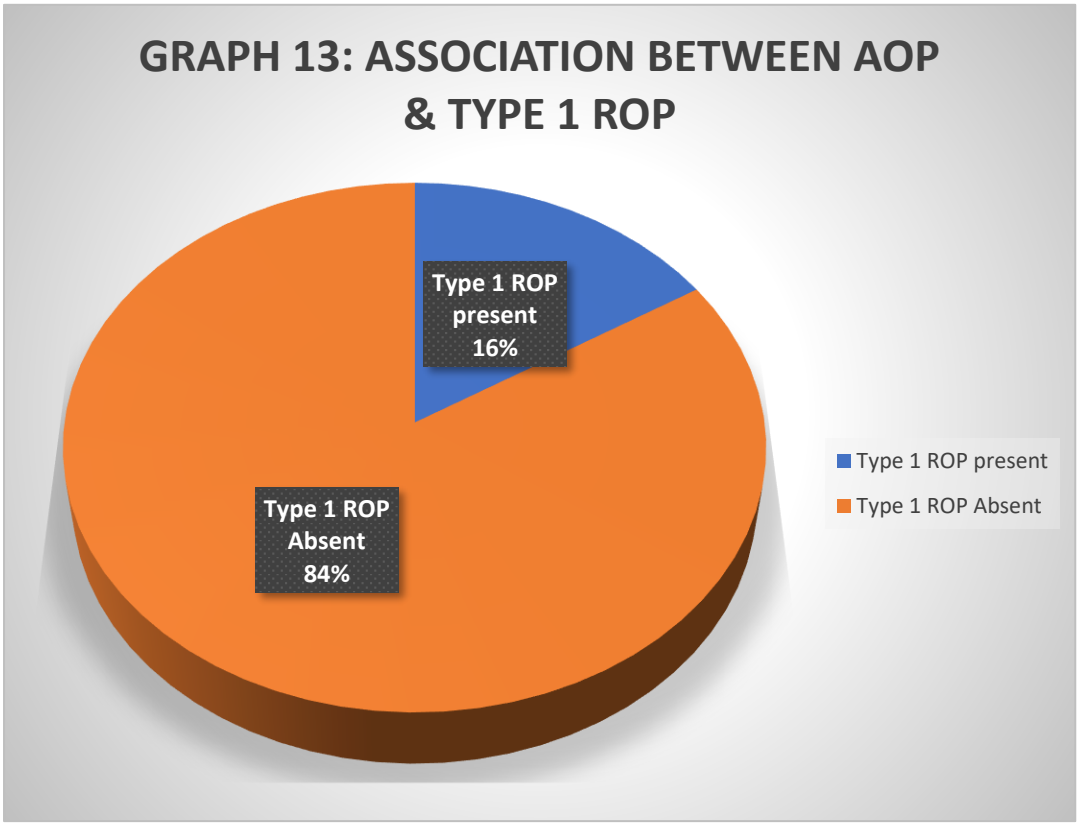


APNOEA OF PREMATURITY

56 of the 263 infants included in this study had AOP. 10 of these 56 developed Type 1 ROP. By Univariate analysis, it was noticed to be having considerable association with the progress to Type 1 ROP. (p-value = 0.0001; $\chi^2 = 14.2210$)

Table 18: Association of AOP and Type 1 ROP

Type 1 ROP	AOP Present	AOP Absent	Total
Present	9 (16.07%)	6 (2.90%)	15
Absent	47 (83.93%)	201 (97.10%)	248
Total	56 (21.29%)	207 (78.71%)	263

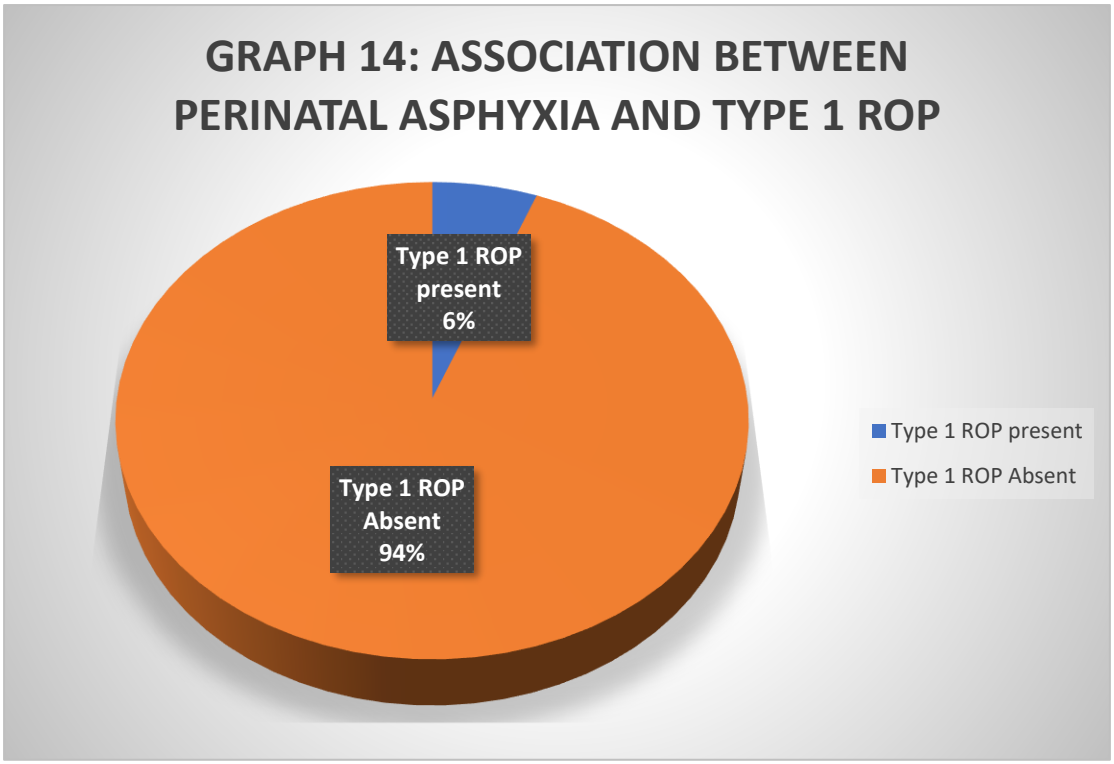


PERINATAL ASPHYXIA

17 of the 263 infants included in this study had Perinatal Asphyxia. 1 of these 17 developed Type 1 ROP. By univariate analysis, it was uncovered to be having major association with the development of Type 1 ROP. (p-value = 0.9740; $\chi^2 = 0.0010$)

Table 19: Association of Perinatal asphyxia and Type 1 ROP

Type 1 ROP	Perinatal Asphyxia Present	Perinatal Asphyxia Absent	Total
Present	1 (5.88%)	14 (5.69%)	15
Absent	16 (94.12%)	232 (94.12%)	248
Total	17 (6.46%)	246(93.54%)	263

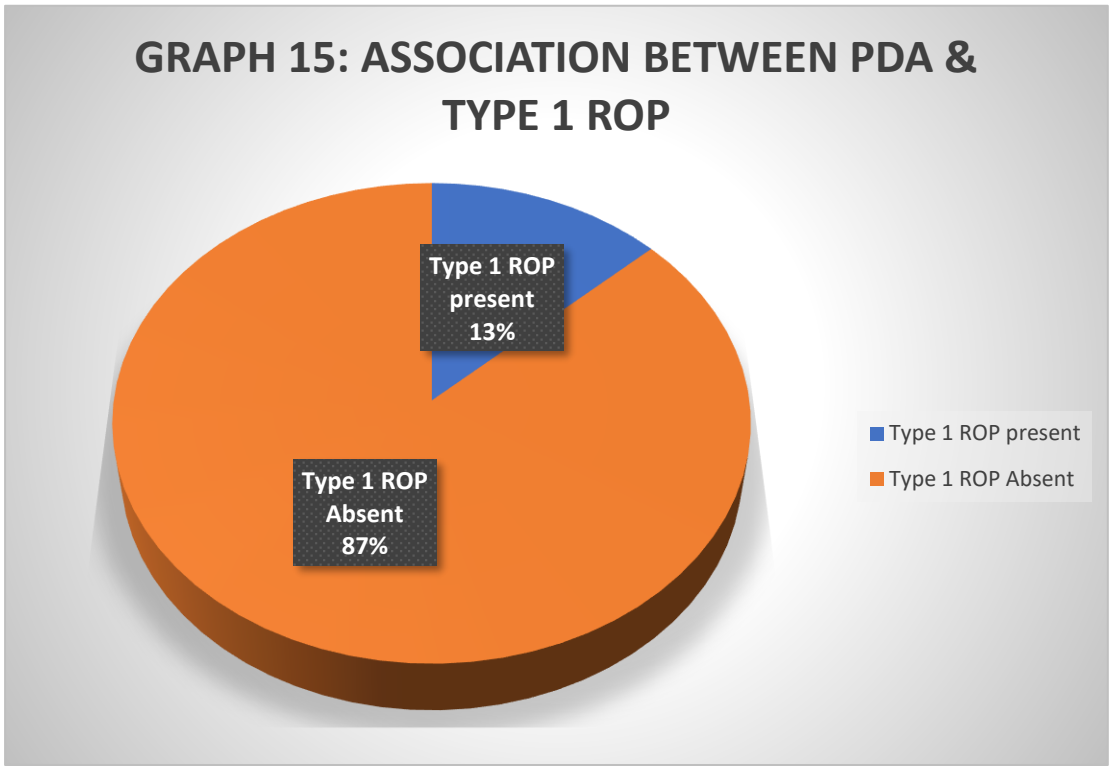


PATENT DUCTUS ARTERIOSUS (PDA)

38 of the 263 infants included in this study had PDA. 5 of these 38 developed Type 1 ROP. By univariate analysis, it was found to have significant association with the development of Type 1 ROP. (p-value = 0.0320; $\chi^2 = 4.5890$)

Table 20: Association of PDA and Type 1 ROP

Type 1 ROP	PDA present	PDA absent	Total
Present	5 (13.16%)	10 (4.44%)	15
Absent	33 (86.84%)	215 (95.56%)	248
Total	38 (14.45%)	225(85.55%)	263

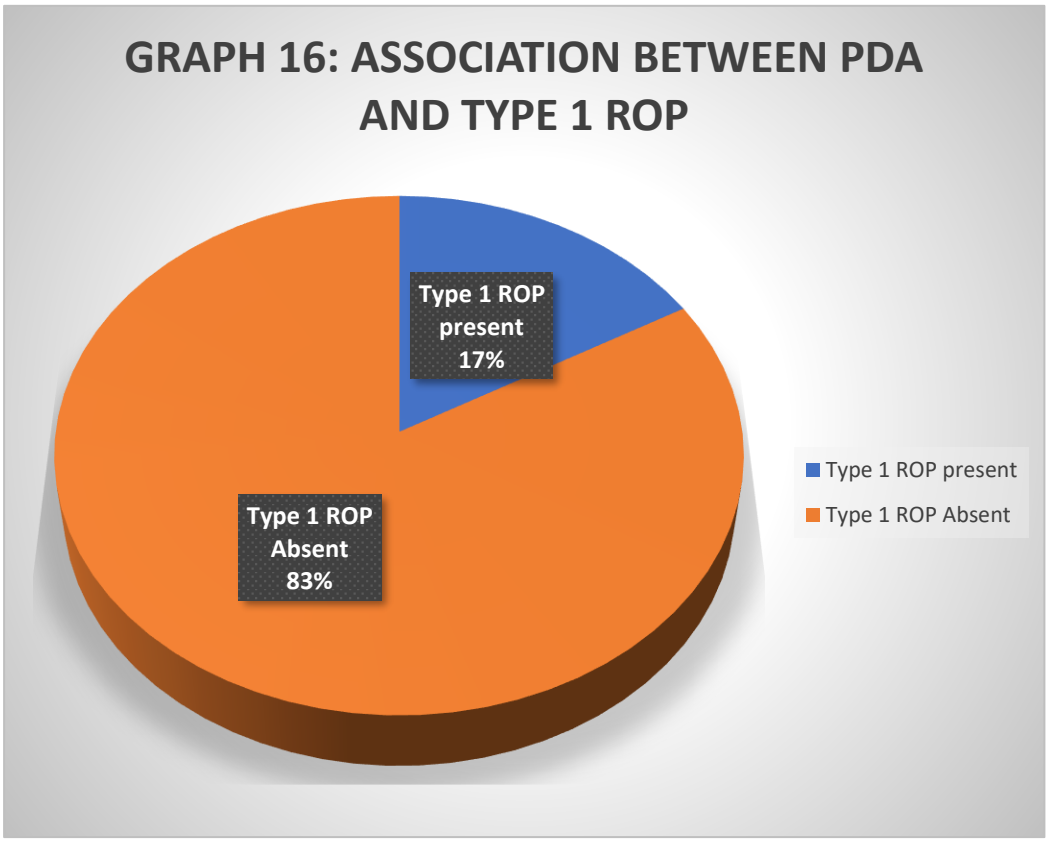


MEDICAL MANAGEMENT OF PDA

In our study, 18 of the infants who developed PDA required treatment. They were managed medically with Indomethacin. 3 of these 18 developed Type 1 ROP. By univariate analysis, it was found to have significant association with the development of Type 1 ROP. (p-value = 0.0380; $\chi^2 = 4.3180$)

Table 21: Association of PDA treatment and Type 1 ROP

Type 1 ROP	PDA treatment given	PDA treatment not given	Total
Present	3 (16.67%)	12 (4.90%)	15
Absent	15 (83.33%)	233 (95.10%)	248
Total	18 (6.84%)	245(93.16%)	263

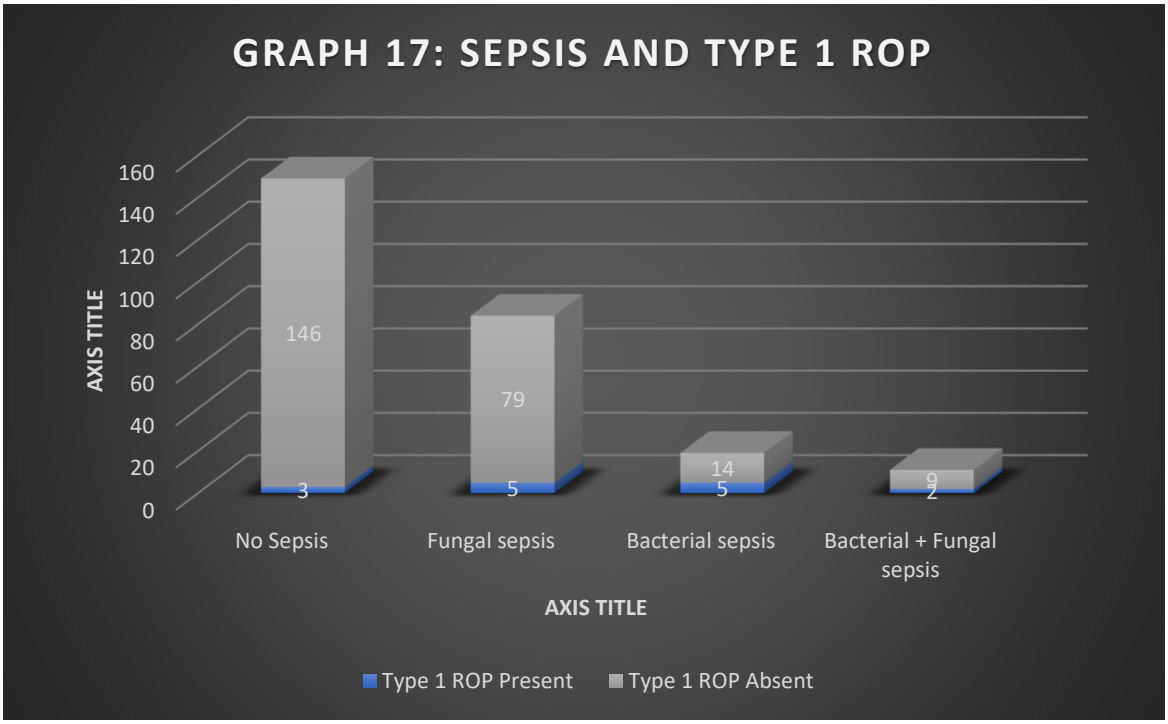


SEPSIS

In our study, 117 infants developed sepsis. 79 had Fungal sepsis, 14 had Bacterial sepsis and 9 developed both. According to univariate analysis, sepsis was an independent risk factor for developing Type 1 ROP. (p-value = 0.0001; χ^2 = 21.9770).

Table 22: Association between sepsis and Type 1 ROP

Sepsis	Type 1 ROP	Total	%	χ^2	p- value
No sepsis	3	149	2.01	21.9770	0.0001*
Fungal Sepsis	5	84	5.95		
Bacterial Sepsis	5	19	26.32		
Both	2	11	18.18		

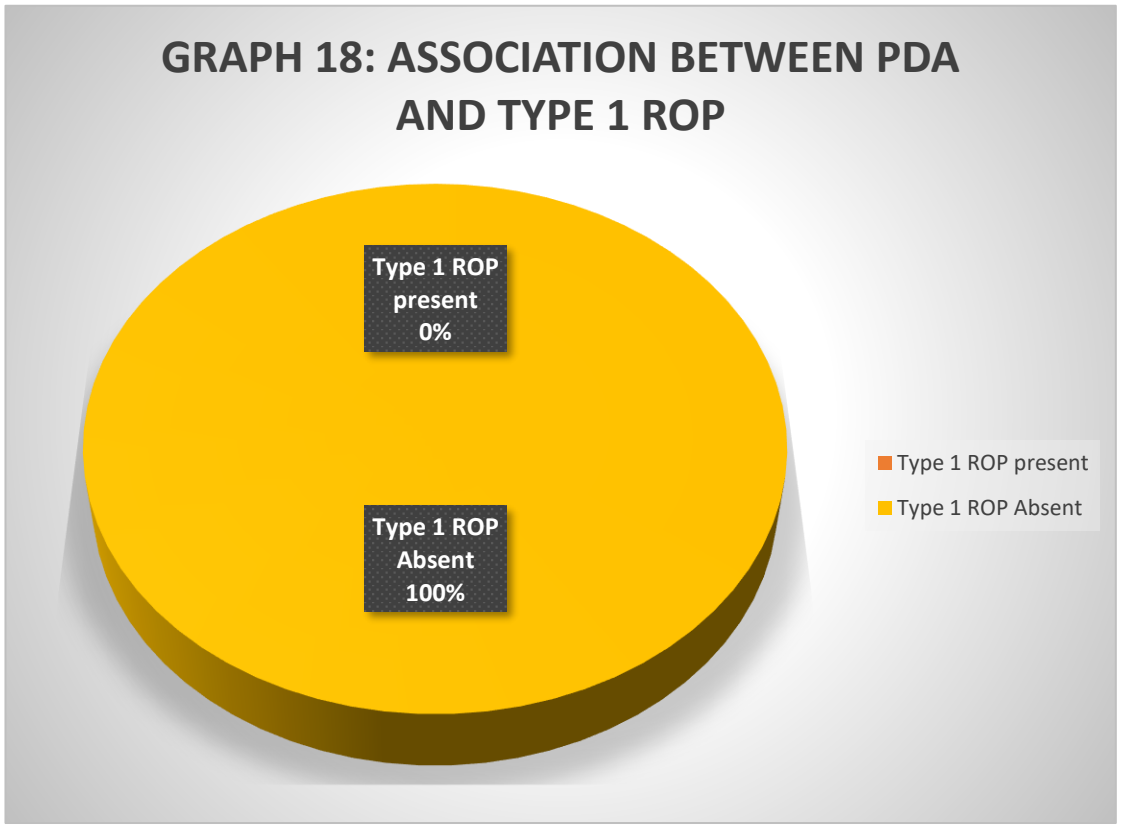


INTRAVENTRICULAR HEMORRHAGE (IVH)

Only one of the 263 infants included in this study had IVH. None developed Type 1 ROP. By univariate analysis, it was found to not have any significant association with the development of Type 1 ROP. (p-value = 0.8050; $\chi^2 = 0.0610$)

Table 23: Association of IVH and Type 1 ROP

Type 1 ROP	IVH present	IVH absent	Total
Present	0	15(5.73%)	15
Absent	1 (100%)	247 (94.27%)	248
Total	1 (0.38%)	262 (99.62%)	263

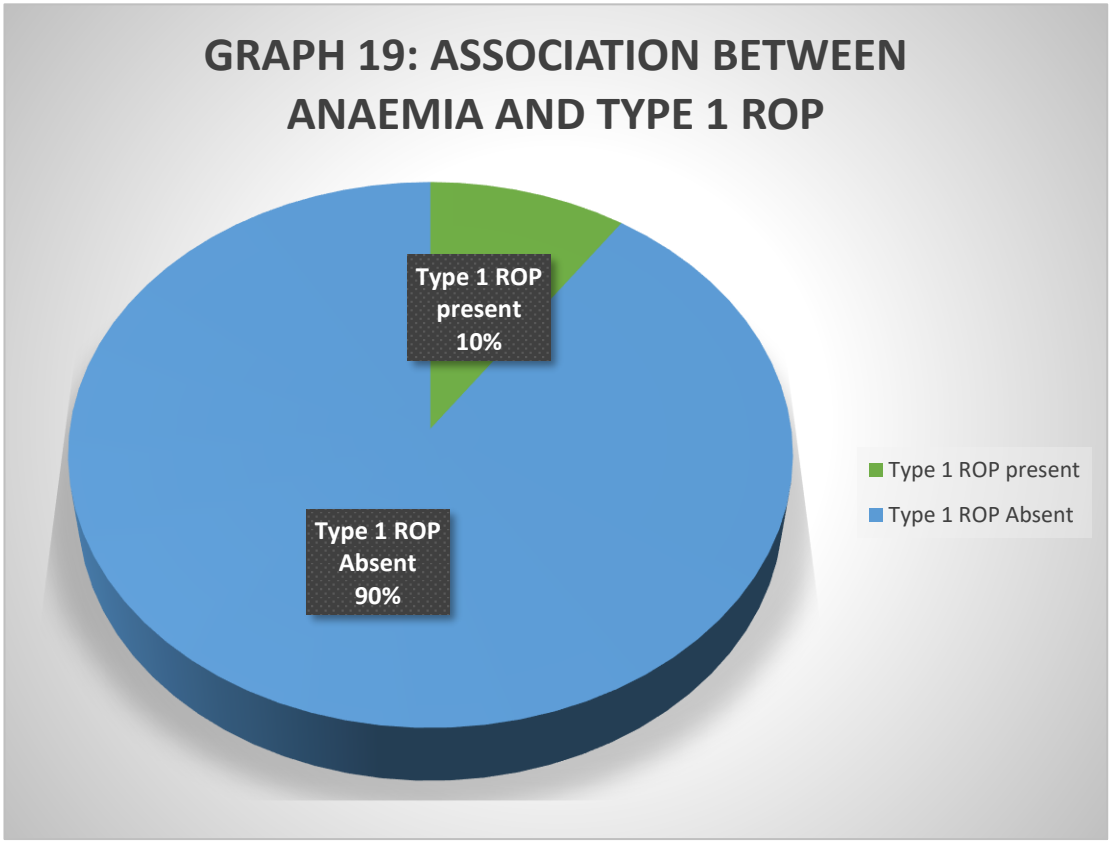


ANAEMIA

31 out the 263 infants included in this study had Anemia. 3 of these 31 developed Type 1 ROP. By univariate analysis, it was found to not have any significant association with the development of Type 1 ROP. (p-value = 0.3100; $\chi^2 = 1.0320$)

Table 24: Association of Anaemia and Type 1 ROP

Type 1 ROP	Anaemia present	Anaemia absent	Total
Present	3 (9.68%)	12 (5.17%)	15
Absent	28 (90.32%)	220 (94.83%)	248
Total	31 (11.79%)	232 (88.21%)	263

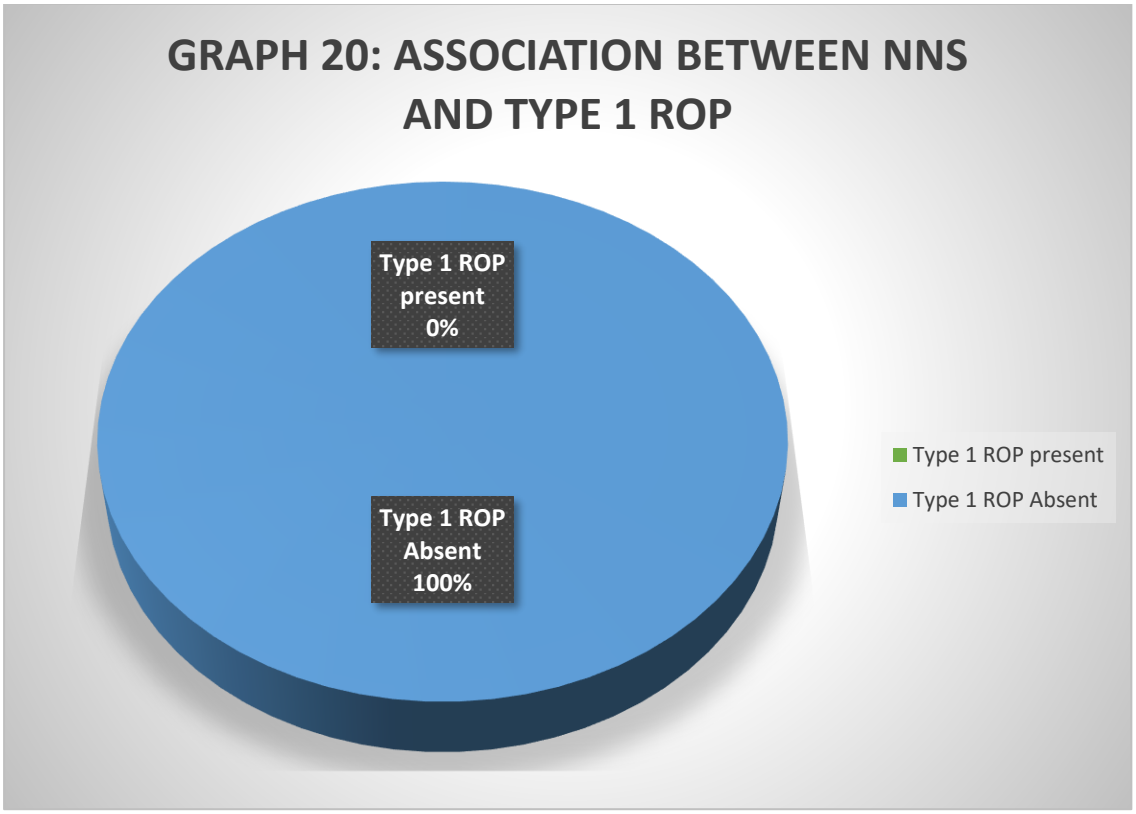


NEONATAL SEIZURES (NNS)

5 out the 263 infants included in this study had neonatal seizures. None Type 1 ROP. By univariate analysis, it was found to not have any significant association with the development of Type 1 ROP. (p-value = 0.5790; $\chi^2 = 0.3080$)

Table 25: Association of NNS and Type 1 ROP

Type 1 ROP	NNS present	NNS absent	Total
Present	0	15 (100%)	15
Absent	5 (100%)	243 (94.19%)	248
Total	5 (1.90%)	258 (98.10%)	263



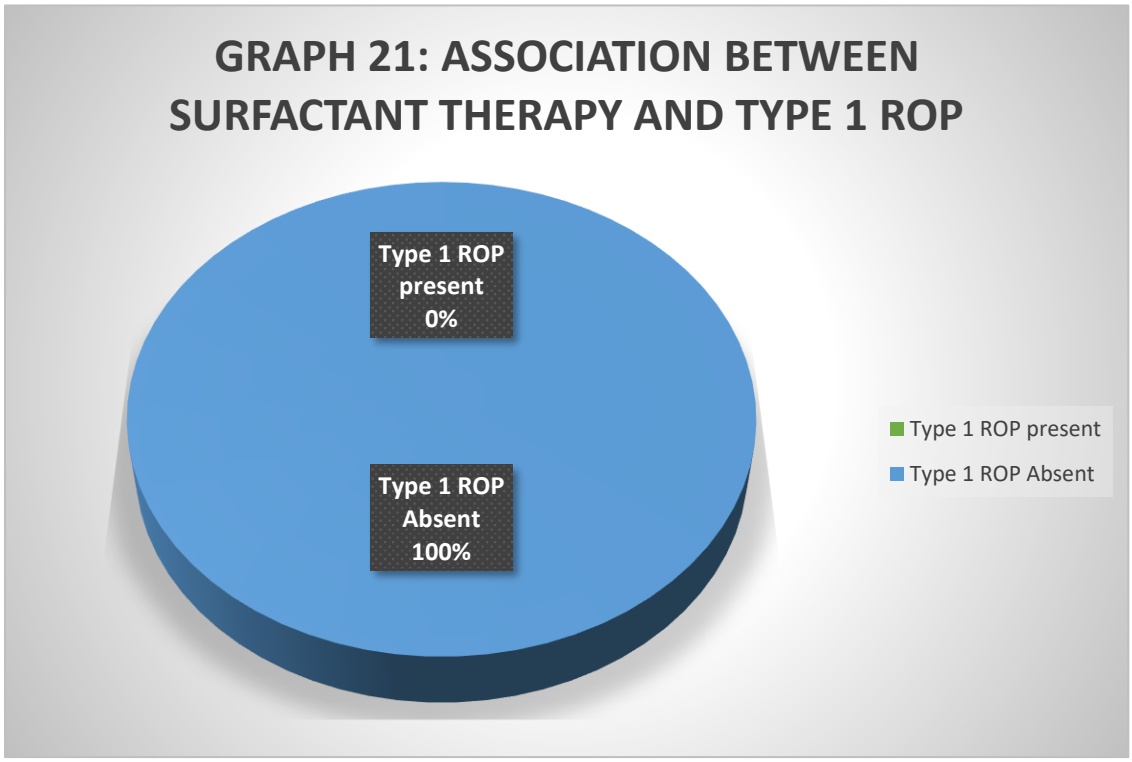
SURFACTANT THERAPY

2 out the 263 infants included in this study required surfactant therapy. Neither of these 2 infants developed Type 1 ROP. By univariate analysis, it was found to not have any significant association with the development of Type 1 ROP.

(p-value = 0.7270; $\chi^2 = 0.1220$)

Table 26: Association of Surfactant therapy and Type 1 ROP

Type 1 ROP	Surfactant therapy given	Surfactant therapy not given	Total
Present	0	15 (5.75%)	15
Absent	2 (100 %)	246 (94.25 %)	248
Total	2 (0.76%)	261(99.24%)	263

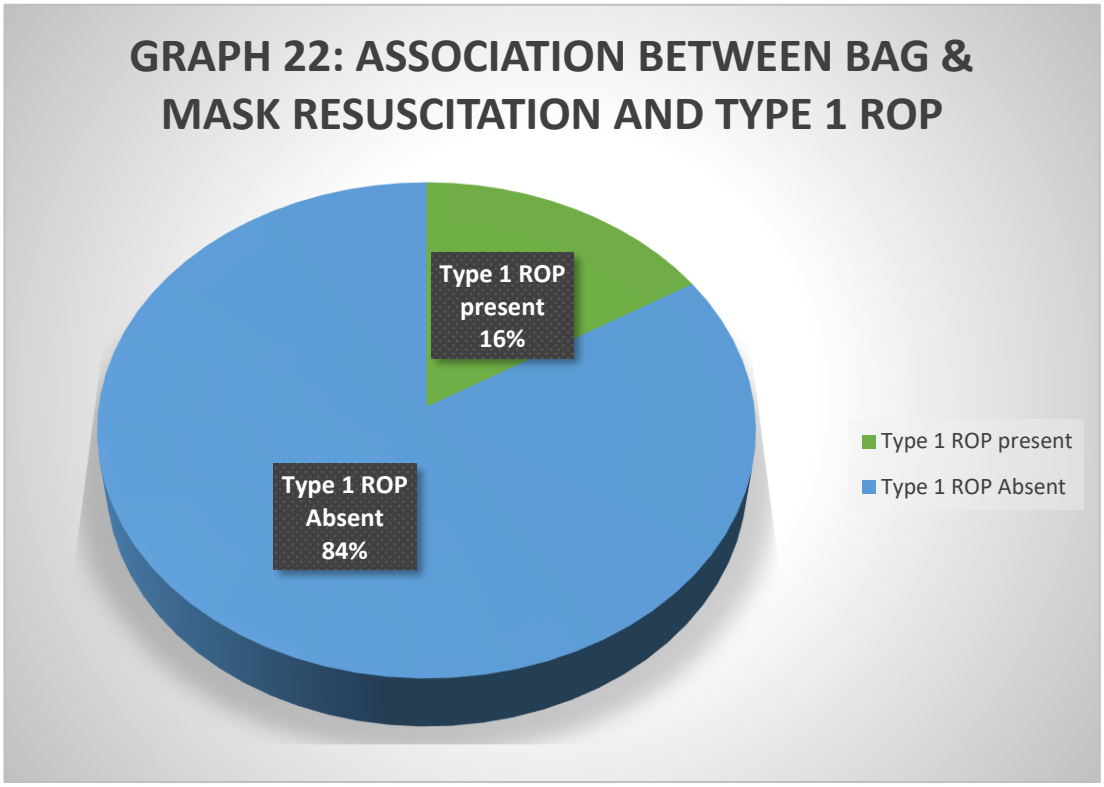


BAG AND MASK RESUSCITATION

37 out the 263 infants included in this study required Bag & Mask resuscitation (B&M). By univariate analysis, it was having a considerable association with the development of Type 1 ROP. (p-value = 0.0030; $\chi^2 = 8.8480$)

Table 27: Association of B & M resuscitation and Type 1 ROP

Type 1 ROP	B&M given	B & M not given	Total
Present	6 (16.22%)	9 (3.98%)	15
Absent	31 (83.78%)	217 (96.02%)	248
Total	37 (14.07 %)	226 (85.93%)	263



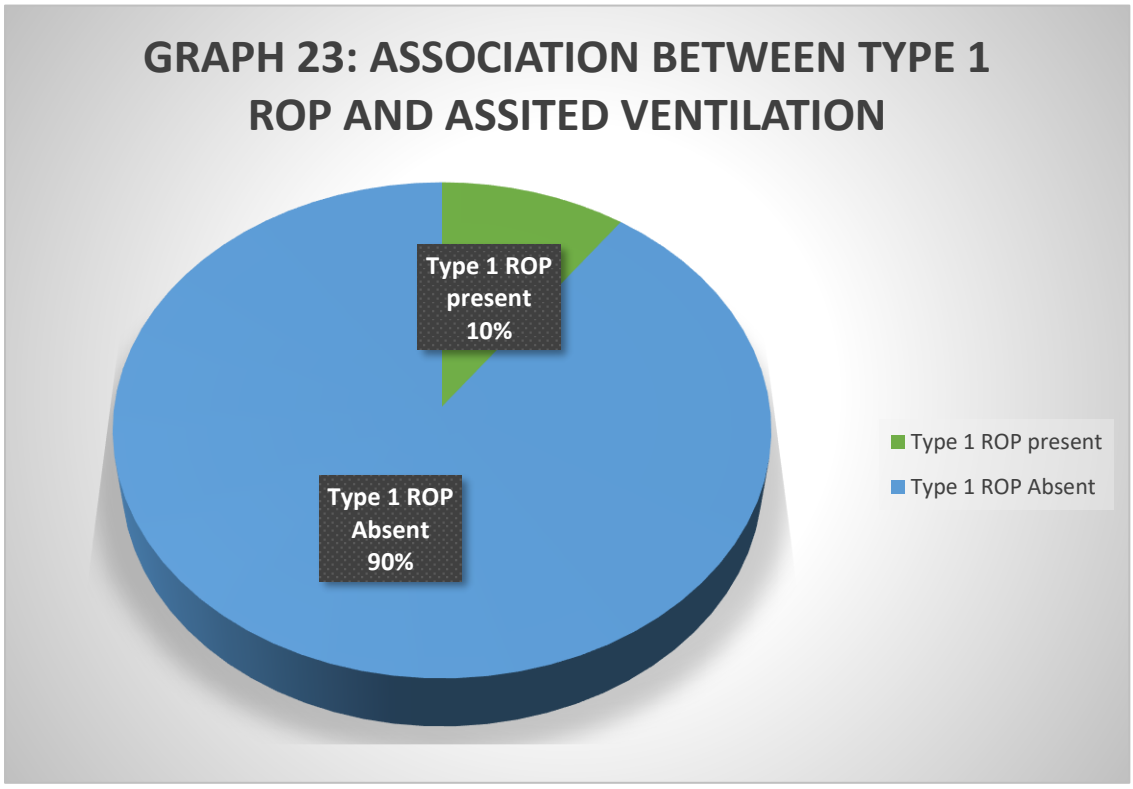
ASSISTED VENTILATION

10 out the 263 infants included in this study required mechanical ventilator support for > 7 days. 1 infant developed Type 1 ROP. By univariate analysis, it was found to not have any significant association with the development of Type 1 ROP.

(p-value = 0.5500; $\chi^2 = 0.3570$)

Table 28: Association of Surfactant therapy and Type 1 ROP

Type 1 ROP	Ventilator > 7 days given	Ventilator 0 – 7 days	Total
Present	1 (10 %)	14 (5.53 %)	15
Absent	9 (90 %)	239 (94.47 %)	248
Total	10(3.80%)	253 (96.20%)	263

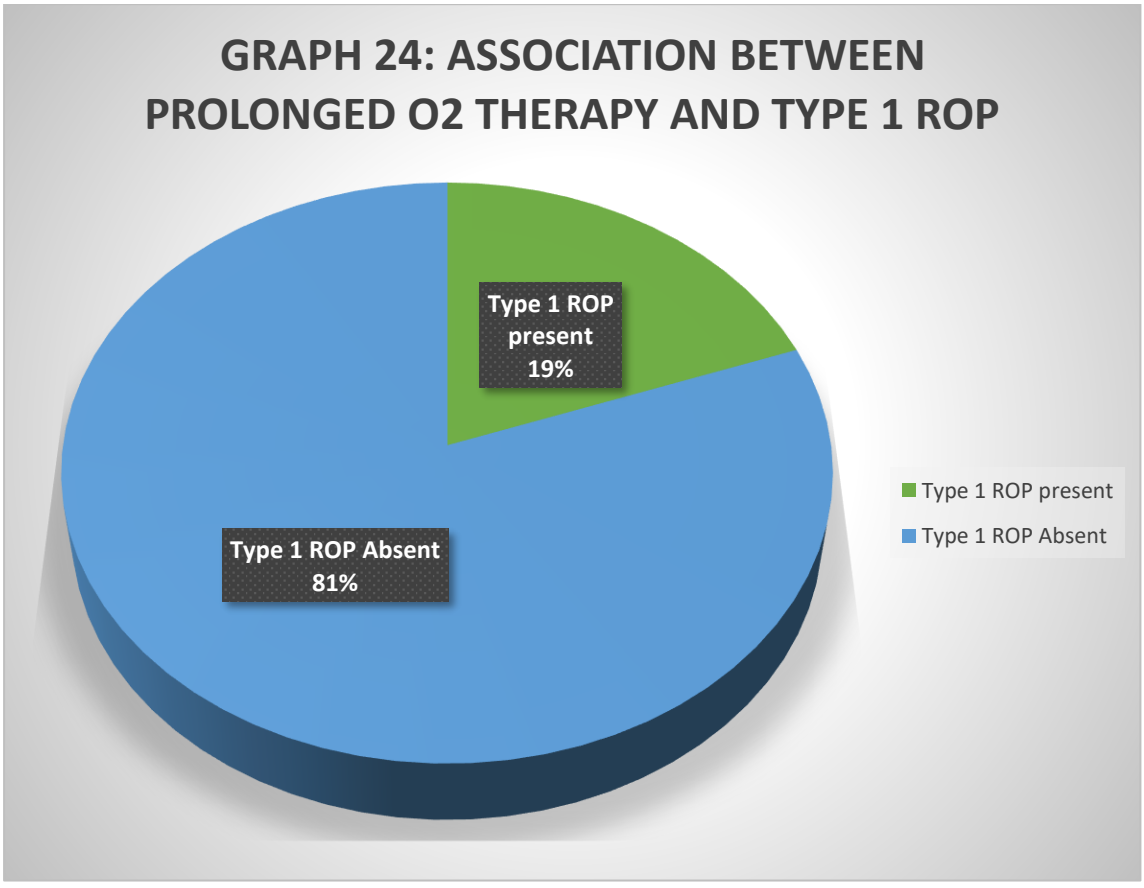


OXYGEN THERAPY

36 out the 263 infants included in this study required prolonged (> 7 days) Oxygen therapy. 7 of these infants developed Type 1 ROP. By univariate analysis, it had a considerable association with developing Type 1 ROP. (p-value = 0.0001; χ^2 = 14.643)

Table 29: Association of Prolonged Oxygen therapy and Type 1 ROP

TYPE 1 ROP	O2 > 7 DAYS	O2 < 7 DAYS	TOTAL
Present	7 (19.44%)	8 (3.52%)	15
Absent	29 (80.56%)	219 (96.48%)	248
Total	36 (13.69%)	227 (86.31%)	263



BLOOD TRANSFUSION

In this study, 84 infants of the 263 included required blood transfusions. 27 required > 5 transfusions and 57 required up to 5 transfusions.

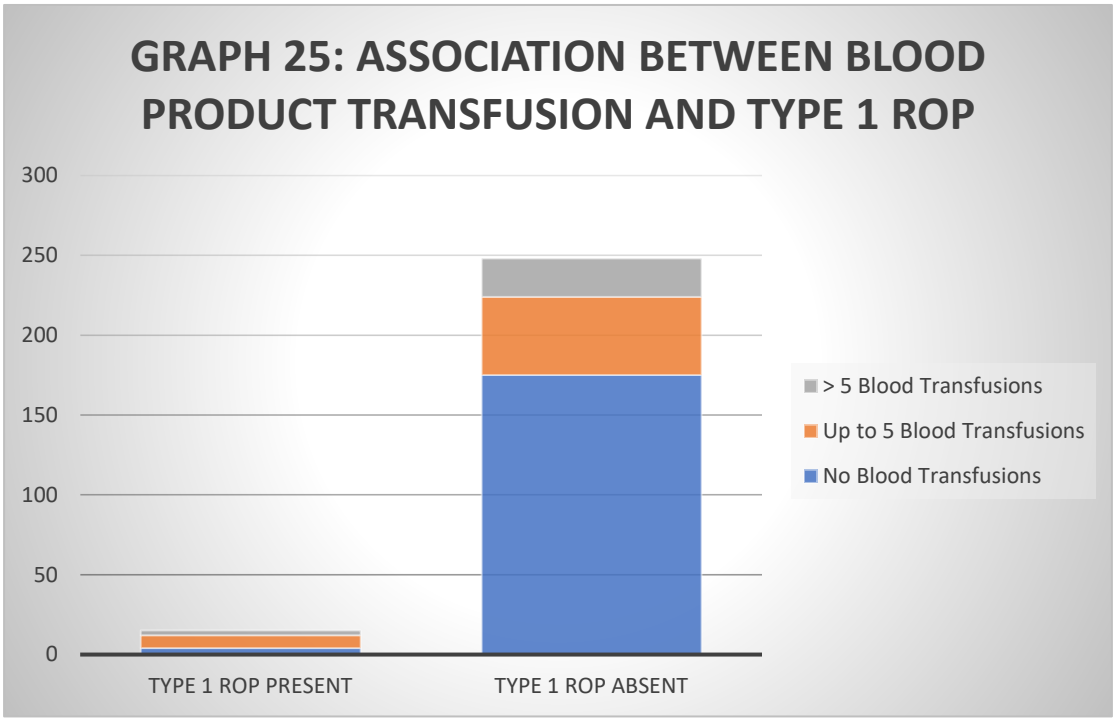
In infants who received up to 5 transfusions – 8 infants developed Type 1 ROP and in infants who received > 5 transfusions- 3 infants developed Type 1 ROP.

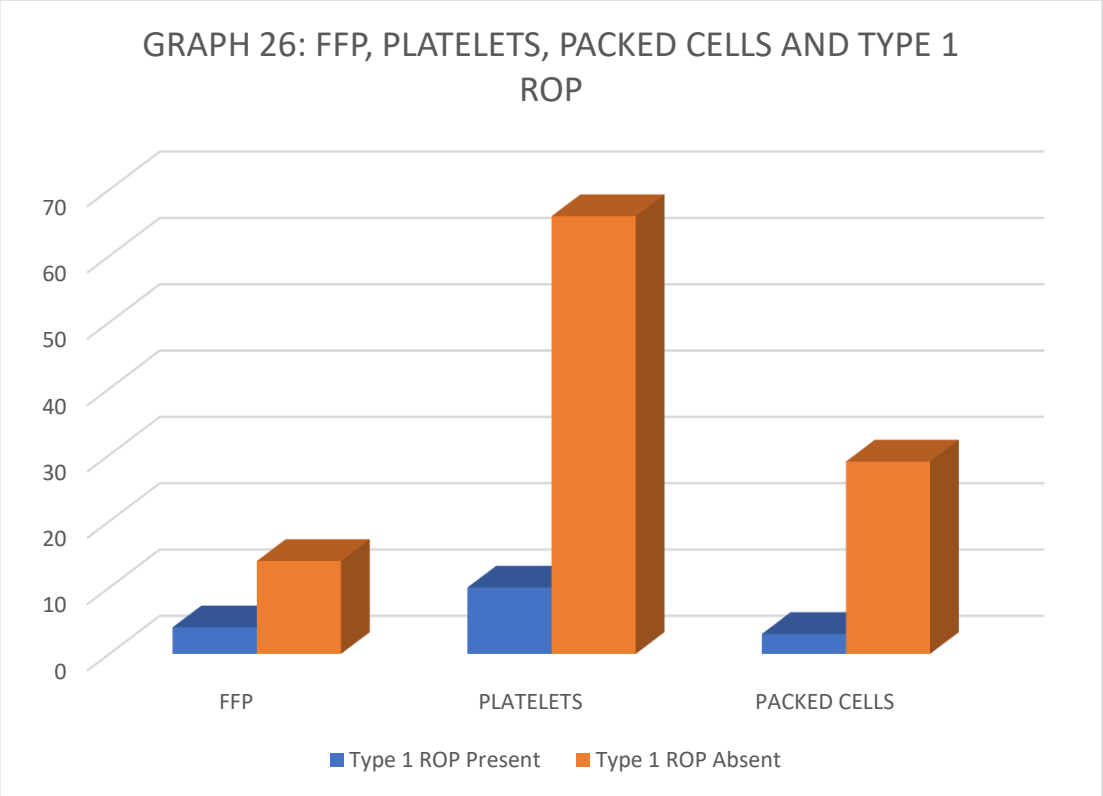
By univariate analysis, transfusion of blood products was having considerable association with the development of Type 1 ROP. (p-value = 0.0020; $\chi^2 = 12.830$)

Table 30: Association of Blood transfusions and Type 1 ROP

Type 1 ROP	**Up to 5 BT given**	**> 5 BT given**	**BT not given**	**Total**
Present	8 (14.04 %)	3 (11.11 %)	4 (2.23 %)	15
Absent	49 (85.96 %)	24 (88.89 %)	175 (97.77%)	248
Total	57 (21.67 %)	27 (10.27 %)	179 (68.06%)	263

FFP, Platelets and Packed cells have been found to be significant risk factors for developmental of Type 1 ROP.


GRAPH 25: ASSOCIATION BETWEEN BLOOD PRODUCT TRANSFUSION AND TYPE 1 ROP
300
250
200
150
100
50
0
TYPE 1 ROP PRESENT
TYPE 1 ROP ABSENT
> 5 Blood Transfusions
Up to 5 Blood Transfusions
No Blood Transfusions


GRAPH 26: FFP, PLATELETS, PACKED CELLS AND TYPE 1 ROP
70
60
50
40
30
20
10
0
FFP
PLATELETS
PACKED CELLS
Type 1 ROP Present
Type 1 ROP Absent

Univariate analysis of the risk factors

Table 31: Univariate analysis of all the risk factors

Risk factor	Yates correction (χ^2)	p- value
Gestational age	24.3270	0.0001*
Birth weight	41.2590	0.0001*
Gender	0.0070	0.9310
Birth Order	1.3650	0.2430
Prenatal steroid use	2.4190	0.4900
Mode of delivery	0.5740	0.4490
Gestational Diabetes	2.2680	0.1320
Maternal Hypertension	5.8830	0.0150*
PPROM	1.0910	0.2960
RDS	2.2430	0.1340
APNOEA of Pre-maturity	14.2210	0.0001*
Peri-natal Asphyxia	0.0010	0.9740
Patent ductus arteriosus	4.5890	0.0320*
PDA treatment	4.3180	0.0380*
Sepsis	21.9770	0.0001*
IVH	0.0610	0.8050
Anaemia	1.0320	0.3100
Neonatal Seizures	0.3080	0.5790
Surfactant use	0.1220	0.7270
Bag and Mask Resuscitation	8.8480	0.0030*
Assisted Ventilation	0.3570	0.5500
Prolonged O2 therapy	14.6430	0.0001*
Blood transfusions (Overall)	12.8300	0.0020*
FFP transfusion	9.8040	0.0020*
Platelets transfusion	11.0440	0.0010*
Packed Cell transfusion	0.9130	0.3390

Multivariate analysis of the risk factors

Table 32: Multiple logistic regression analysis by demographic variables

Risk factor	Adjusted Odds ratio	p-value	95% Confidence Interval
Gestational age			
Up to 28 weeks	Ref.		
29-32 weeks	0.71	0.6850	0.13 – 3.83
32-34 weeks	0.23	0.2650	0.02 – 3.08
≥ 35 weeks	0.00	0.9970	-
Birth weight			
< 800 gm	Ref.		
800 – 1000 gm	0.48	0.5340	0.05 – 4.97
1000 – 1250 gm	0.68	0.7590	0.06 – 7.92
1251 - 1500g	0.05	0.0640	0.00 – 1.19
>1500g	0.04	0.0490*	0.00 – 0.98
Gender	0.49	0.8900	0.14 – 1.66

Table 33: Multiple logistic regression analysis by Mother related parameters

Risk factor	**Adjusted Odds ratio**	**p-value**	**95% Confidence Interval**
Parity			
Up to 28 weeks	Ref.		
29-32 weeks	0.71	0.6850	0.13 – 3.83
32-34 weeks	0.23	0.2650	0.02 – 3.08
≥ 35 weeks	0.00	0.9970	-
Prenatal steroids			
< 800 gm	Ref.		
800 – 1000 gm	0.48	0.5340	0.05 – 4.97
1000 – 1250 gm	0.68	0.7590	0.06 – 7.92
1251 - 1500g	0.05	0.0640	0.00 – 1.19
>1500g	0.04	0.0490*	0.00 – 0.98
Mode of delivery			
GDM	0.49	0.8900	0.14 – 1.66
Maternal HTN	4.14	0.0240*	1.21 – 14.22
PPROM	0.52	0.5640	0.06 – 4.70

Table 34: Multiple logistic regression analysis by Neonatal parameters

Risk factor	**Adjusted Odds ratio**	**p-value**	**95% Confidence Interval**
RDS	0.51	0.3950	0.11 – 2.43
AOP	2.96	0.1390	0.70 – 12.45
Perinatal asphyxia	0.65	0.7280	0.06 – 7.18
PDA	5.85		
PDA treatment	0.46		
Sepsis			
Fungal sepsis	1.00	1.0000	0.16 – 6.36
Bacterial sepsis	17.04	0.0190*	1.61 – 180.67
Bacterial + fungal sepsis	2.32	0.5660	0.13 – 40.74
IVH	-	-	-
Anaemia	0.36	0.2850	0.06 – 2.33
Neonatal seizures	-	-	-
Surfactant	-	-	-
Bag & Mask ventilation	2.94	0.1650	0.64 – 13.47
Assisted ventilation	0.19	0.2660	0.01 – 3.59
Prolonged O2 therapy	4.31	0.0920	0.79 – 23.62
Blood transfusion (overall)			
Up to 5 transfusions	1.47	0.7450	0.14 – 15.19
>5 transfusions	0.01	0.0001*	-
FFP	2.83	0.1380	0.72 – 11.21
Platelets	4.64	0.0170*	1.32 – 16.27
Packed cells	0.72	0.6510	0.17 – 3.02

We have tried to use multiple logistic regression analysis using all the factors, but the sample size was small for analysis for Type 1 ROP.

TREATMENT

Of the 263 infants included in this study, any stage ROP was seen in 64 infants. Of these 64 infants, 15 progressed to Type 1 ROP mandating treatment and the rest regressed over the follow-ups.

Treatment was given by frequency doubled Nd: YAG LASER photocoagulation and intravitreal anti-VEGF injection.

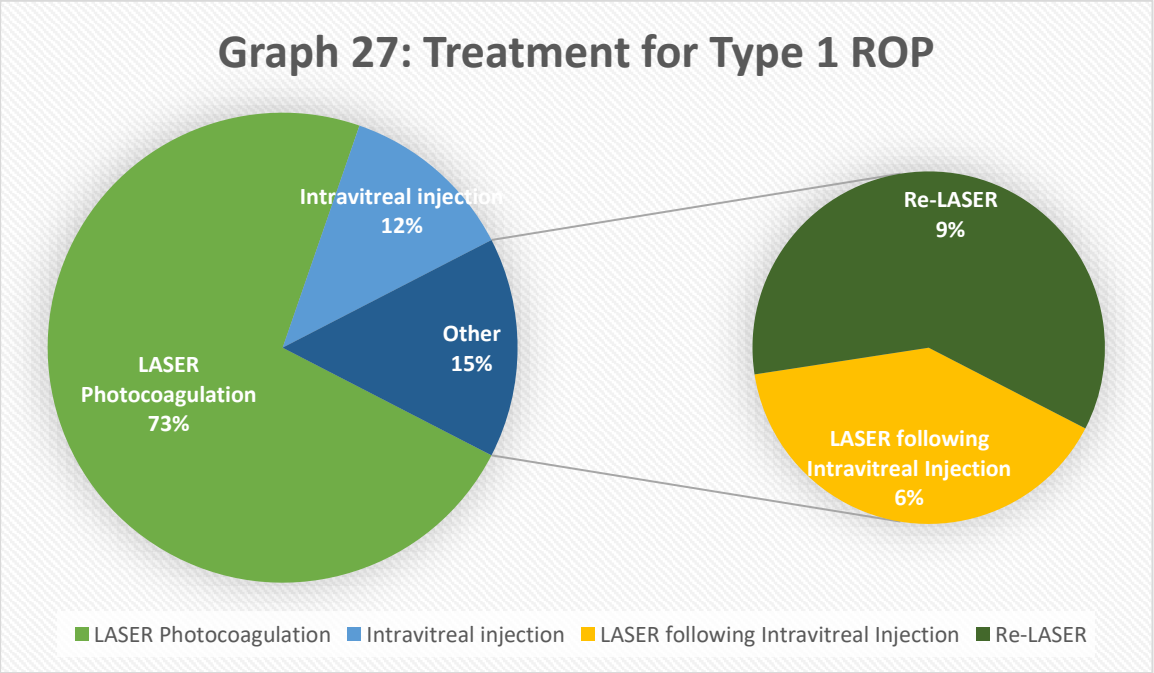
Of the 15 infants diagnosed with Type 1 ROP, LASER photocoagulation was delivered to 24 eyes. 3 eyes of 2 infants had to be re lasered as there were skip areas found during the follow-up.

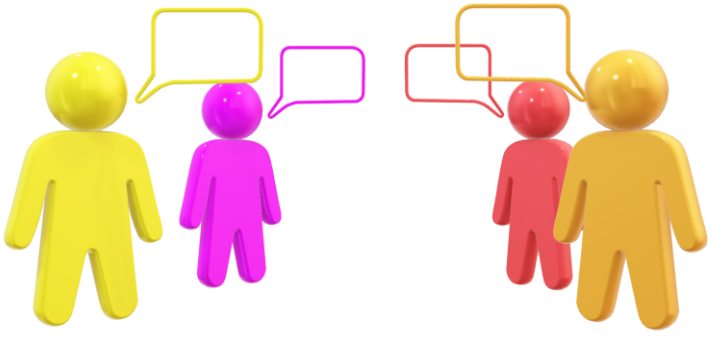
In 2 eyes, Intravitreal Bevacizumab injection was given and in 2 eyes, Intravitreal Ranibizumab injection was given. 2 eyes of one infant needed LASER following injection.

Overall, the outcome has been favourable in all the cases.

Table 35: Treatment given to infants

Type 1 ROP	LASER PHOTOCOAGLATION	INTRAVITREAL INJECTION	Re-LASER
28 eyes of 15 infants	24 eyes of 15 infants	4 eyes	3 eyes





DISCUSSION

DISCUSSION

Retinopathy of prematurity (ROP) is a vaso-proliferative disorder of the premature infants. ROP has emerged as the major cause of preventable blindness among children[171], leading to lifelong visual impairment and blindness.

Around 15 million children are born prematurely. Around 53,000 suffer from sight-threatening ROP that requires treatment and around 20,000 of them end up having blindness.[4] Most of the preterm births worldwide are from India.[172]

A study done in South India showed the prevalence of blindness in children to be 6.5 per 10,000 children.[173] It is economically important and also a severe social implication, which in terms of blind years is very long. Among the avoidable causes of impaired vision in childhood, ROP totals the highest. LBW and GA at birth stand to be the most critical risk factors causing ROP, particularly Type 1 ROP.

We screened babies admitted to our NICUs with birth weight ≤ 2000g and gestation age at birth ≤ 34 weeks. Infants with birth weight >2000g and gestation age at birth > 34 weeks with risk factors. It follows the guidelines of Government of India for prevention of Childhood Blindness.

INCIDENCE

There have been a lot of developments recently in the health care infrastructure in low- and middle-income countries, especially India. With better health care and better equipped Neonatal Care Units, there has been enhanced survival of premature, LBW infants. Also, there has been an increasing ROP incidence, so is that of treatable ROP (Type 1 ROP).

The overall incidence of any ROP in the present study was found to be 24.33% and that of Type 1 ROP to be 5.7% with only two cases of APROP. It is of the current knowledge that, APROP occurs especially among smaller and more immature neonates.

One of the 2 infants who developed APROP, had a birth weight of 1130grams and the other infant had a birth weight of 790 grams and gestational age at birth in both the infants was 28 weeks.

In the CRYO-ROP study, the incidence of ROP in a group of premature infants born with a birth weight <1251 grams was 65.8% and for infants less than 1000grams, it was 81.6%[19]. In the ETROP study, that was done 15 years ago, the overall incidence of ROP was found to be 68% in infants weighing <1251 grams at birth.

The incidence of more-severe ROP (pre-threshold) was 36.9% among infants with ROP from the ETROP Study, whereas in the CRYO-ROP study, it was 27.1%[19].

A review of literature reveals that the incidence and severity of ROP increase with decreasing GA & BW.

Table 36: Incidence of Type 1 ROP in Indian and International studies

Study	Inclusion criteria		Incidence
	Gestational Age	**Birth Weight**	
Nair *et al*., 2003[26]	≤32 weeks	< 1250 grams	10.16%
Gupta *et al*., 2004[32]	≤35 weeks	<1500 grams	5%
Vasavada *et al*.,2017[174]	< 34 weeks	< 1700 grams	10.29%
Ahuja *et al*., 2018[175]	≤36 weeks	≤1900 grams	13.2%
Dwivedi *et al*.,2019[176]	< 37 weeks	< 2000 grams	14.2%
Goyal *et al*., 2019[177]	< 34 weeks	< 1700 grams	9.95%
Warad *et al*., 2019[178]	< 36 weeks	< 2000 grams	11.81 %
Present Study	**≤34 weeks**	**< 2000 grams**	**5.7%**
INTERNATIONAL STUDIES			
Wani *et al*.,2010 [22]	< 34 weeks	<1500 grams	7.8%
Xu *et al*., 2013 [179]	< 34 weeks	< 2000 grams	6.8%
Bas *et al*., 2015[180]	≤32 weeks	≤1500 grams	8.2%
Freitas *et al*.,2018[181]	< 32 weeks	< 1500 grams	5.0 %
TR-ROP study., 2018[182]	≤32 weeks	≤1500 grams	6.7%
G-ROP study, 2018[183]	≤ 30 weeks	<1501grams	6.1%
Akkawi *et al*., 2019[184]	< 32 weeks	< 1500 grams	11.3 %
Castellon *et al*., 2019[185]	≤ 34 weeks	< 1750 grams	28.8%
Braimah *et al*., 2020[186]	< 37 weeks	< 2000 grams	1.8%

The incidence of Type 1 ROP studied elsewhere India was 1.8 – 11.3%.[22,25,179–186] Study from the Indian subcontinent reveals the incidence of Type 1 ROP to be 5 – 14.2%. [26,32,174–177].

A study done by Warad *et al*., reported the prevalence to be 11.81%[178]. The incidence of Type 1 ROP in our study was 5.7 %, which was comparable to few studies internationally and a study done by Gupta *et al*., in India, but low compared to other studies in the Indian scenario.

Nair *et al*., stated a total incidence of ROP as 25.4%; severe ROP as 10.16%. They studied 59 infants with GA at birth ≤32wk or BW < 1250gms.[26] A study conducted by Gupta *et al*., reported an overall incidence ROP as 21.7% and that of Type 1 ROP as 5%. They studied 60 infants with GA at birth ≤ 35weeks or BW ≤1500gms.[32] Dutta *et al*., reported an overall incidence of ROP as 21%.[187]

RISK FACTORS

In our study Gestational age, Birth weight, Maternal Hypertension, apnoea of prematurity, Patent Ductus Arteriosus and its medical treatment, Sepsis, Bag and Mask resuscitation, oxygen therapy for > 7 days, Blood transfusion (FFP / Platelets), were found to be significant risk factors on univariate analysis.

By multivariate analysis, Birth weight amongst prenatal factors, maternal hypertension among other mother related factors; Neonatal sepsis (Bacterial infection) and more than 5 blood transfusions (Platelets > Packed Cells > FFP) are independent risk factors for the development of Type 1 ROP.

1. Birth Weight and Gestational age:

In our study both low birth weight ($p = 0.001$) and prematurity ($p = 0.001$) are noted as significant factors for developing Type 1 ROP.

The BW of the Type 1 ROP babies ranged from 716-1670 gm (mean 1126.40 ± 241.15 gm), while that of any ROP and non-ROP babies ranged from 750-3100 gm (mean 1619.96 ± 432.63 gm). LBW showed substantial association with high incidence ($p = 0.001$) of Type 1 ROP. Type 1 ROP incidence of in infants with BW ≤ 1500gm was 11.38 %.

The GA of infants with Type 1 ROP was 28 -31 wks (29.6 ±1.45 weeks), while that in non-ROP babies was 24-40 wks (33.6 ± 2.77 weeks). In infants born ≤ 34 wks GA, the incidence of Type 1 ROP was 7.85%. GA was a major risk factor for the development of Type 1 ROP ($p=0.001$) in this study.

2. Maternal Hypertension

Out of the 263 infants screened, 98 were born to mothers who had Hypertension during pregnancy. 10 (10.20%) of these 98 infants developed Type 1 ROP. According to this study, it is a significant risk factor, according to univariate (p=0.0150) and multivariate analysis.

In their study by Shah *et al*., the infants who developed Type 1 ROP and requiring treatment were 28 of the 564 screened infants. They found preeclampsia to be significant risk factor by univariate and also by multivariate analyses.[21]

A study by Zhu *et al*., on the association between Hypertensive diseases in pregnancy and ROP, stated the need for additional studies and that no clear association was found between maternal hypertensive disorders and severe ROP.[95]

3. Apnea of prematurity (AOP), Bag & Mask Resuscitation:

Out of 263 babies screened, 56 babies had AOP and 9(16.07%) developed Type 1 ROP. AOP was noted to be a major risk factor for the development of Type 1 ROP in this study (p = 0.0001).

Kim *et al*[62], found apnoea to be an independent risk factor for development of severe ROP. Further, increased frequency of apnoeic attacks increased the progression from pre-threshold ROP to threshold ROP.

A higher incidence of hypoxemia and episodes of apnoea requiring bagging was found among babies having severe ROP than in a control group[30,58].

In a study by Chen *et al*.,[61] they found apnoea to be an independent risk factor for developing ROP. Its appropriate management might reduce the incidence of ROP.

4. PDA and its medical management:

In our study, 38 (14.45%) of the 263 infants had PDA. Of these, 5 (13.16%) developed severe ROP. Out of the 38 infants who had PDA, only 18 required management.

PDA was managed medically by administration of Indomethacin. Amongst the infants treated with Indomethacin, 3 (16.67%) developed severe ROP. Both PDA itself and treatment of PDA with Indomethacin have emerged as independent risk factor by univariate analysis.

A study by Viejo *et al*.,[188] found a statistically significant association between PDA and development of severe ROP but they found an inverse relation on multiple logistic regression analysis when they considered gestational age. Tsui *et al*.,[140] also that there was significant association between treatment of PDA with indomethacin and its association with severe ROP on univariate analysis but not on multivariate analysis, when considering other variables.

In our study, PDA itself (p=0.0320) and its treatment with Indomethacin (p=0.0380) have been found to have similar association, i.e., significant on univariate analysis, but not on multivariate analysis.

5. Sepsis

In our study, 117 (43.35%) infants of the 263 included, developed sepsis. 31.9% (84 infants) developed Fungal sepsis, 7.22% (19 infants) developed Bacterial sepsis and 4.18% (11 infants) developed combined sepsis (Bacterial + fungal sepsis).

Most common Fungal causative organism was *Candida glabrata*. Sepsis has been found to be a significant factor in this study both by univariate and multivariate analyses.

A study by Manzoti *et al*., stated the association between Fungal sepsis in ELBW infants to be significant for developing threshold ROP.[189] ELGAN study found that late neonatal sepsis itself is an independent risk factor for developing threshold ROP.[190]

It was found in a Swedish cohort study that low platelets itself predisposed the infant to develop sepsis. And that multiple thrombocytopenia episodes predisposed the infant to develop APROP.[127]

In this study, Fungal sepsis has been found to be significant risk factor by univariate analysis, but bacterial sepsis was found to be a substantial and independent factor even by multivariate analysis.

6. Blood transfusion

During blood transfusion, there is replacement of HbF by HbA which causes rapidly increasing oxygen availability to the retina thereby causing ROP.[123]

In our study, 84 infants (31.94%) needed blood transfusions. 11(25.15%) of these 84 infants developed Type 1 ROP.

FFP transfusion was given to 18 infants (6.84%), 4 (22.2%) of who developed type 1 ROP. Platelets were transfused in 76 infants (28.90%), 10 infants 13.16%) amongst them developed Type 1 ROP.

Platelet transfusion and FFP transfusions were independent risk factors significant for development of Type 1 ROP.

7. Oxygen therapy:

In our study, oxygen therapy for > 7 days was noted to be a significant risk factor for the developing Type 1 ROP on Chi-square analysis (p=0.0001), on univariate analysis and on multivariate analysis. Out of 263 infants screened, 36 were given O2 for more than 7 days and 22 (61.11%) babies developed Type 1 ROP.

The link between Type 1 ROP and supplemental oxygen has been confirmed already. Gunn *et al*., analyzed LBW survivors and found a significant association between, duration of oxygen therapy and the severe grade of cicatricial disease.[58] Different studies have evaluated the effect of different concentrations of oxygen saturation levels and the incidence of ROP like the STOP- ROP, BOOST trial, SUPPORT-ROP, COT study.[67,191–193]

Kinsey observed that the concentration of the administered oxygen was significantly associated with occurrence of ROP in infants with birth weight < 1200gm. When comparing mean arterial oxygen levels of normal infants with that of infants with ROP, Kinsey found differences only in babies of LBW and only arterial oxygen levels > 150mmHg[56]. A study by Zapata *et al*., mentions the use of devices in the NICU for delivery of automatically adjusted fraction of oxygen as per the requirement.[194] Use of such devices could be really helpful to prevent unmonitored exposure of oxygen to the infant.

Table 37: Comparison of oxygen as a risk factor of ROP in different studies

Study	**p-value**
Halimic *et al*.,[195]	< 0.05
Rekha *et al*., [27]	0.005
Present study	0.0001

Other risk factors:

In our study, we did not find use of steroids, mode of delivery, PPROM, phototherapy, RDS, Neonatal Seizures, perinatal asphyxia, to be associated with Type 1 ROP as found in other studies.

Limitations of the study:

The sample size is small to assess /identify the role of all the risk factors if they can cause Type 1 ROP independently on multivariate analysis and also over the period of years.

CONCLUSION

CONCLUSION

1. The current study reveals the status of Type 1 ROP at a tertiary care centre.

2. The incidence of Type 1 ROP in the current study is 5.7%.

3. Of the 263 infants, 64 infants had any stage ROP, 6 were in Stage 1 (6.25%), 45 were in Stage 2 (70.31%), 13 were in Stage 3 (21.87%) 2 developed APROP.

4. The birth weight of Type 1 ROP infants ranged from 716-1670 gm (mean 1126.40 ± 241.15 gm), while that of non-ROP infants ranged from 1100-2100 gm (mean 1642.80 ± 216.60 gm). LBW was appreciably associated with an increased incidence of Type 1 ROP(p=0.001). The incidence of Type 1 ROP in infants with BW < 1500 grams at was 11.38%.

5. The GA at birth among Type 1 ROP infants varied from 28 -31 wks (29.6 ±1.45 weeks), of non-ROP babies varied from 24-40 wks (33.6 ± 2.77 weeks). Low gestational age was significantly associated factor causing development of Type 1 ROP. The incidence of Type 1 ROP in infants < 34 weeks was found to be 7.85%.

6. On Univariate analysis gestational age, birth weight, maternal hypertension, apnea of prematurity, patent ductus arteriosus and its medical management, neonatal sepsis, bag & mask resuscitation, oxygen therapy for > 7 days and >5 blood transfusions were found to be significant risk factors for development of Type 1 ROP.

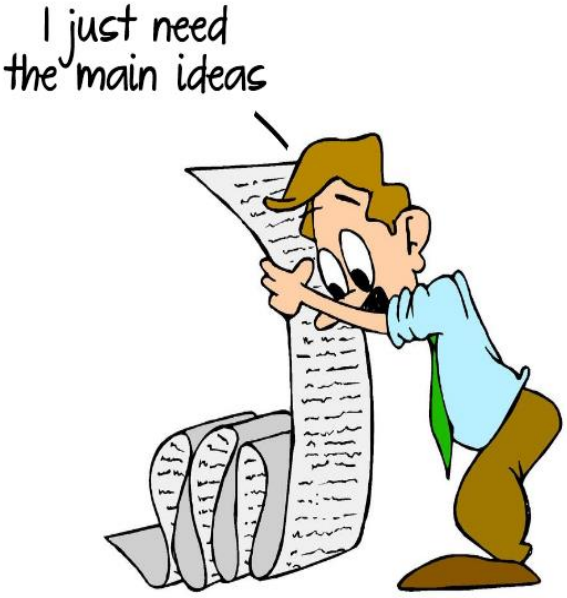
7. On multivariate analysis, Low birth weight among antenatal factors, maternal hypertension among maternal risk factors and in neonatal factors- Sepsis (mainly bacterial) and > 5 blood transfusions (Platelet > packed cells > FFP) were found to be independent risk factors significant for developing Type 1 Retinopathy of Prematurity.

8. The disease regressed in all the infants treated by LASER and by Intravitreal injection.

9. In our opinion, the effective management of Type 1 Retinopathy of Prematurity occurs at different levels, starting at the level of the Neonatologist, the NICU staff, the timely screening, counselling and management by the Ophthalmologist.

10. Consistent screening programmes with norms of BW < 2000 grams and GA at birth < 34 weeks or both and birth weight more than 2000 grams and those with GA at birth > 34 wks in conjunction with other risk factors are at the discretion of the treating neonatologist and the ophthalmologist.

11. Alongside an effective screening, an effective management of the amount of O_2 delivered and the decline of episodes of apnea and effective management of neonatal comorbidities are also required.



SUMMARY

SUMMARY

A one-year longitudinal study was conducted to know the incidence of Type 1 ROP, correlate it with the risk factors causing it and the treatment outcomes of infants admitted to the NICUs of KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi.

263 infants satisfied the inclusion criteria and were enrolled in the study. The incidence of any ROP was 24.33 % (64) and that of Type 1 ROP in the study was 5.7%. Out of the 64 infants, only 6 infants (6.25%) developed stage I ROP, 45 infants (70.31%) developed stage II ROP, 13 infants (21.87 %) developed stage III ROP and 1(1.56%) infant developed APROP.

The mean birth weight of the Type 1 ROP babies was 1126.40 ± 241.15 gm, while that of non-ROP babies was 1619.96 ± 432.63 gm. Lower birth weight was significantly associated with Type 1 ROP.

Average gestational age at birth was 29.65 weeks. 5 of 19 infants born with GA at birth < 28 weeks, 9 of 97 infants born at GA 29 – 32 weeks, 1 of 77 infants born at GA 33 – 34 weeks and none of the infants with GA > 34 weeks developed Type 1 ROP. By univariate and multivariate analyses, Gestational age at birth was found to be a significant risk factor for the development of Type 1 ROP.

There was no relation between Gender distribution and Type 1 ROP. 9 of 155 males had Type 1 ROP and 6 of 108 screened females had Type 1 ROP.

Birth order was not a significant risk factor for the development of Type 1 ROP according to this study.

Like other studies, administration of antenatal steroids was protective against the development of Type 1 ROP.

There was no significant difference in the different modes of delivery and any significant association with the development of Type 1 ROP in infants screened in this study.

Gestational Diabetes Mellitus was found to be a non-significant in the development of Type 1 ROP in infants included in this study.

Gestational Hypertension was found to be a significant risk factor for the development of Type 1 ROP both by univariate and multivariate analyses ($p=0.0150$; $\chi^2= 5.8830$). 10 (10.2%) of the 98 infants born to mothers having Maternal HTN developed Type 1 ROP.

Only 1 infant of the 43 infants who were born to mothers who were having PPROM, developed Type 1 ROP. There was no significant association between PPROM and Type 1 ROP.

Unlike other studies, RDS was not significantly associated with the development of Type 1 ROP in our study. (p=0.1340, χ^2 =2.2430).

Apnoea of Prematurity (AOP) was found to have a significant association with the development of Type 1 ROP. (p=0.0001, χ^2 =14.2210). 9 of 56 infants who developed AOP had also developed Type 1 ROP.

Perinatal asphyxia was found to be significantly associated with the development of Type 1 Retinopathy of Prematurity (p=0.9740, χ^2=0.0010). Type 1 ROP was seen in one of the 17 infants who developed Perinatal Asphyxia.

PDA and its medical management with Indomethacin have been significantly associated with the development of Type 1 ROP. Both by univariate and multivariate analyses it was found to be significant. PDA was seen in 38 of the 263 infants screened and only 5 of them developed Type 1 ROP. 3 of the 15 infants treated with Indomethacin for PDA have developed Type 1 ROP.

Sepsis has emerged as an independent factor for developing Type 1 ROP. Both by univariate and multivariate analyses, it was found to be significantly associated to develop Type 1 ROP. (p=0.0001).

None of the 263 cases screened had Intraventricular Hemorrhage.

31 infants of the 263 screened had Anaemia. Only 3 of them developed Type 1 ROP. It was not found to have any significant relation to developing Type 1 ROP.

None of the cases screened had Neonatal Seizures.

2 cases amongst 263 received surfactant. But none developed Type 1 ROP. There was no significant association between Surfactant therapy and Type 1 ROP.

Bag and mask resuscitation was done in 37 infants. 6 (16.22%) developed Type 1 ROP. 31 did not develop Type 1 ROP. By univariate analysis, it was associated with Type 1 ROP but by multivariate analysis, it did not have a significant association with Type 1 ROP.

10 of the 263 infants screened required ventilator support. Only one of the 10 infants developed Type 1 ROP. By univariate analysis, it was not having any significant association with Type 1 ROP.

Prolonged O2 therapy (> 7 days) was given for 36 of the 263 infants. 7 (19.44%) developed Type 1 ROP. It was found to have a significant association with Type 1 ROP.

Blood transfusions (> 5 units) were associated with developing Type 1 ROP according to this study. A more significant association was seen with FFP than with Platelet transfusion than with Packed cell transfusion.

2 infants, who had APROP were treated with an intravitreal anti-VEGF injection. One required LASER later as ROP recurred after a few weeks.

24 eyes of 15 infants underwent LASER. 3 required releaser due to skip areas. Overall, there was a regression in all cases.

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ANNEXURE I

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed – to- be- University)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (GoI)
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Ref: MDC/DOME/04 **Date: 24/11/2018**

To,

PG student in Ophthalmology,
J.N.Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"A ONE YEAR PROSPECTIVE STUDY TO ASSESS THE INCIDENCE, RISK FACTORS AND TREATMENT OUTCOME OF TYPE I RETINOPATHY OF PREMATURITY IN INFANTSADMITTED TO NICUs OF KLES DR.PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELAGAVI",** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Arathi Darshan)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Roopa M Bellad)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

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ANNEXURE II

CONSENT FOR PARTICIPATION IN RESEARCH STUDY

STUDY ID NO: _____

Parent / Guardian of

_____

You are invited to participate in our research study entitled " A ONE YEAR PROSPECTIVE STUDY TO ASSESS THE INCIDENCE, RISK FACTORS AND TREATMENT OUTCOME OF TYPE I RETINOPATHY OF PREMATURITY IN INFANTS ADMITTED TO NICUs OF KLES DR.PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELAGAVI" conducted by investigator with reg. no BK0118005 , Post Graduate in M.S. OPHTHALMOLOGY under the guidance of Dr._____, Department of Ophthalmology, JAWAHARLAL NEHRU MEDICAL COLLEGE, Belagavi.

Respected Parent / Guardian we request you to enrol your ward to participate in our study as he/she is eligible to do so.

Your ward's participation in this study is voluntary and your decision to / not to participate in the study will not affect your relationship with JAWAHARLAL NEHRU MEDICAL COLLEGE. If you decide to participate (ward) you are free to withdraw at any time.

Purpose of the study: The purpose of this study is to know the incidence of Type 1 Retinopathy of Prematurity (ROP), to correlate it with maternal and neonatal risk factors and measure its treatment outcomes. Better awareness of this will help in identifying the infants at risk of developing Type 1 ROP and to assess early treatment outcomes to prevent blindness.

Procedure involved :

If you agree (ward) to enrol yourself in the study, I will enquire about your baby's mode of delivery, any problems encountered during/after delivery, any other risk factor concerning the mother or baby for development of Retinopathy of Prematurity from you and the hospital records.
Then I will be dilating the baby's eyes by instilling dilating drops into the eyes.
Your child will then be examined by Indirect Ophthalmoscopy and the posterior segment evaluated for the presence of Type 1 ROP. In case your infant has Type 1 ROP, intervention by Laser Ablation or Intravitreal anti-VEGF injection is carried out after taking consent from you and the treatment outcomes are assessed.

Benefits: Results will help to study the incidence, risk factors and treatment outcomes of Type 1 ROP in infants and to assess the treatment outcomes.
Risks: Laser treatment is fairly safe but rare serious side effects reported in the literature include- exudative retinal detachment, no response to therapy, cataract development and rarely Phthisis.
Treatment of Type I ROP that meets the definition of aggressive posterior ROP(APROP) or Type I ROP in zone I with intravitreal injection of

Bevacizumab or Ranibizumab has the following risks- lens touch, infection of the cavity of the eye, retinal detachment, initial regression with later recurrence in the eye. The systemic side effects of the drug include –gastrointestinal haemorrhage, late healing of wounds, possible affection of cognitive development.

Alternatives :

If parent/ Guardian is not willing to take part in the study, his / her treatment or any other further investigations the patient wants to undergo, in future, in KLE will not be affected by his / her decision.

Voluntary participation/withdrawal :

Taking part in this study is voluntary. I may choose not to take part in this study, or if I decide to take part I can later change my mind and withdraw from the study. My decision will not change the present or future health care or other services that I receive. The study doctor or the sponsor may stop my participation in this study. I will tell of any important new findings that may change my willingness to continue to take part. If I choose not to take part in the study my infant will receive the standard treatment for infants with my infant's condition.

Costs :

The screening for ROP is free. However, if the baby needs treatment by laser or by intravitreal injection for TYPE I ROP then the necessary costs according to the hospital rules have to be paid.

Compensation :

In the event that my infant becomes injured as a result of taking part in this study, treatment will be offered to me. No reimbursement, compensation or free medical care is given.

Confidentiality:
All information collected about my infant during the course of the study will be kept confidential to the extent permitted by the law. The code numbers will identify my infant in this research record. Information from this study may be published but my identity will be confidential in any publication.

QUESTION:
If any enquiries in the future or in case of research-related injury illness, you may contact the following person.

1) **PRINCIPAL INVESTIGATOR:**
2) **GUIDE:**
3) **CO-GUIDE:**
4) **CO – GUIDE: Even if you have any queries in future, you may contact the following person**
5) **Dr. ROOPA BELLAD M.D., DCH,**

CONSENT TO PARTICIPATE IN RESEARCH TRIAL

I, Parent / Guardian of _____ voluntarily agree for the participation of my ward as a subject of this study. By signing this consent form I am not giving up any of my legal rights. I may withdraw from the study anytime. I am signing the consent after having read or been read for me in my vernacular language, including the risks and benefits and having all my questions answered.

Subject

Name

:_____

Parent / guardians Name

:_____

Signature / Left Thumb impression:

_____

Witness name

:_____

Signature / Left Thumb impression:

_____

Investigators name :

Signature

:_____

Date : **Place :**

Name of Guide:

Signature of Guide : _____

Co- Guide:

Signature of co-Guide: _____

Co- Guide :

Signature of co-Guide: _____

ANNEXURE-III

DATA COLLECTION INSTRUMENT

"A ONE YEAR PROSPECTIVE STUDY TO ASSESS THE INCIDENCE, RISK FACTORS AND TREATMENT OUTCOME OF TYPE I RETINOPATHY OF PREMATURITY IN INFANTS ADMITTED TO NICUs OF KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELAGAVI"

Baby of: **Infant Number:**

Date of Examination: **Hospital Number:**

Address: **Date of admission:**

Mobile No.: **Date of birth:**

Pre-examination evaluation:

Age(weeks) : Gestational Chronological

Corrected Age (Gestational Age + Chronological):

Birth Weight: gm

Sex : (1 – MALE, 2 – FEMALE)

Birth Order : (1 – Single, 2 - Twins, 3 - Triplets)

Indication for ROP Screening in this Infant

- ☐ **Birth weight < 2000gms**
- ☐ **Gestational Age < 34 weeks**
- ☐ **Weight > 2000 gm and GA 34 to 36 weeks with risk factors.**
- ☐ **Infants with an unstable clinical course who is at high risk.**

Maternal Risk Factors:

Prenatal Steroids : (1- Yes, 2- No)

Mode of Delivery : (1- Normal, 2 – Forceps, 3 – Caesarian, 4 – Vacuum)

Gestational Diabetes : (1- Yes, 2- No)

Maternal Hypertension: (1- Yes, 2- No)

: (1 – Preeclampsia, 2 – Eclampsia, 3 – PIH)

PPROM : (1- Yes, 2- No)

Others : (1- Yes, 2- No)

Neonatal Risk Factors:

1) **Respiratory Distress Syndrome** : ☐ **(1- Yes, 2- No)**
2) **Apnoea of Prematurity** : ☐ **(1- Yes, 2- No)**
3) **Perinatal Asphyxia** : ☐ **(1- Yes, 2- No)**
4) **Patent Ductus Arteriosus** : ☐ **(1- Yes, 2- No)**
   Hemodynamically Stable : ☐ **(1- Yes, 2- No)**
5) **Proven Sepsis** : ☐ **(1- Yes, 2- No)**
   Fungal / Bacterial : ☐ **(1- Fungal, 2- Bacterial)**
6) **Intraventricular Hemorrhage** : ☐ **(1- Yes, 2- No)**
7) **Anaemia** : ☐ **(1- Yes, 2- No)**
8) **Neonatal seizures** : ☐ **(1- Yes, 2- No)**
9) **Others** :

Treatment

1) **Surfactant Therapy** : ☐ **(1- Yes, 2- No)**
   Total how many doses : ☐ **(= no. of doses)**
2) **Bag & Mask resuscitation** : ☐ **(1- Yes, 2- No)**
3) **Ventilated** : ☐ **(1- Yes, 2- No)**
   How many days : ☐ **(= no. of days)**
4) **Oxygen Therapy** : ☐ **(1- Yes, 2- No)**
   How many doses : ☐ **(= no. of days)**
5) **Blood transfusion** : ☐
   How many units : **FFP** ☐ **Platelets** ☐ **Packed Cells** ☐
6) **Others:**

Investigations:

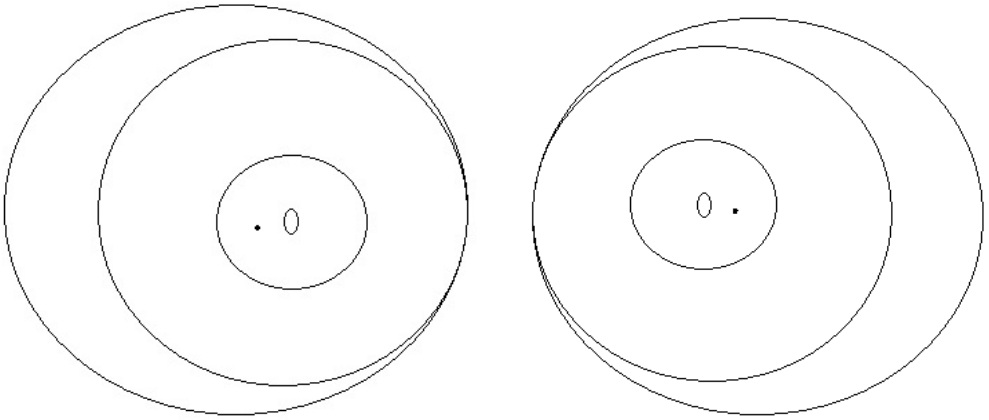
1) Chest X-ray PA view :
2) ECHO cardiograph :
3) Blood Culture :
4) Maximum CRP :
5) Cranial USG :
6) Arterial Blood Gas :
7) Max pO2 / FiO2 :
8) Haemoglobin :

Initial Examination

ANTERIOR SEGMENT	RIGHT EYE	LEFT EYE
Active iris vasculature		
Tunica Vasculosa Lentis		
Rigid Pupil		
Others		

Posterior Segment

RIGHT EYE **LEFT EYE**



	ZONE			1	2	3			ZONE				1	2	3		
STAGE	**0**	**1**	**2**	**Type 1**	**APROP**	**4A**	**4B**	**5**	**STAGE**	**0**	**1**	**2**	**Type 1**	**APROP**	**4A**	**4B**	**5**

RIGHT EYE	(1 – Yes, 2 – No)	LEFT EYE
	Dilatation of vessels	
	Iris vessels dilatation	
	Pupil rigidity	
	Vitreous haze	
	Retinal haemorrhages	
	Pre-Plus	
	Plus	

TREATMENT:(Observation=1, Laser = 2, Intra-Vitreal injection of anti-VEGF = 3)

RIGHT EYE : ☐ **LEFT EYE :** ☐

FOLLOW UP AFTER: **Date:**

COMMENTS:

EXAMINING DOCTOR: **SIGNATURE**

FOLLOW UP PROFORMA

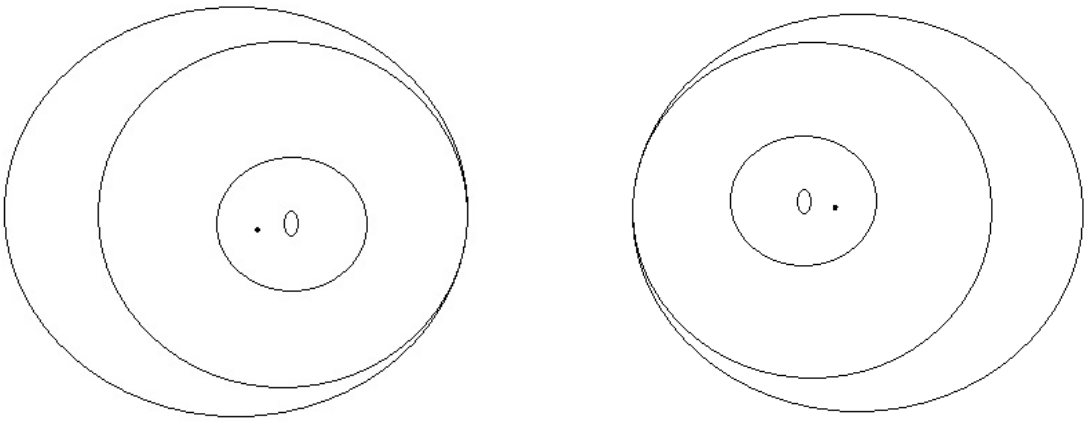
Name : Baby of _____
Visit number: Date of Examination :

Chronological Age: Post Conceptional Age :

ANTERIOR SEGMENT	RIGHT EYE	LEFT EYE
Active iris vasculature		
Tunica Vasculosa Lentis		
Rigid Pupil		
Others		

Posterior Segment

RIGHT EYE **LEFT EYE**



	ZONE			1	2	3			ZONE				1	2	3		
STAGE	0	1	2	Type 1	APROP	4A	4B	5	STAGE	0	1	2	Type 1	APROP	4A	4B	5

RIGHT EYE	(1 – Yes, 2 – No)	LEFT EYE
	Dilatation of vessels	
	Iris vessels dilatation	
	Pupil rigidity	
	Vitreous haze	
	Retinal haemorrhages	
	Pre-Plus	
	Plus	

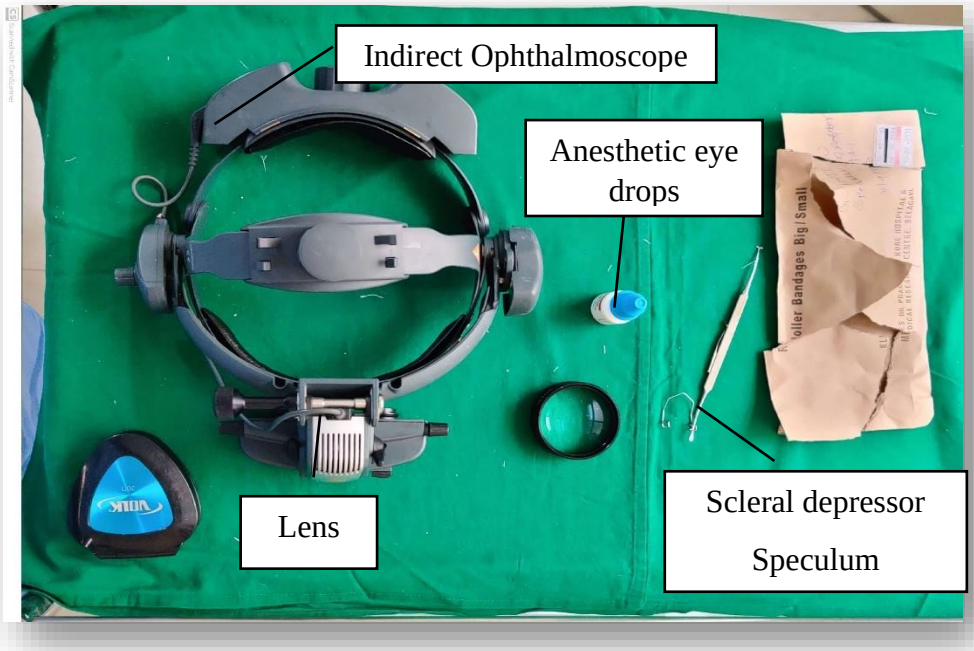
TREATMENT:
(Observation=1, Laser = 2, Intra-Vitreal injection of anti-VEGF = 3)
RIGHT EYE : ☐ **LEFT EYE :** ☐

FOLLOW UP AFTER: **Date:**

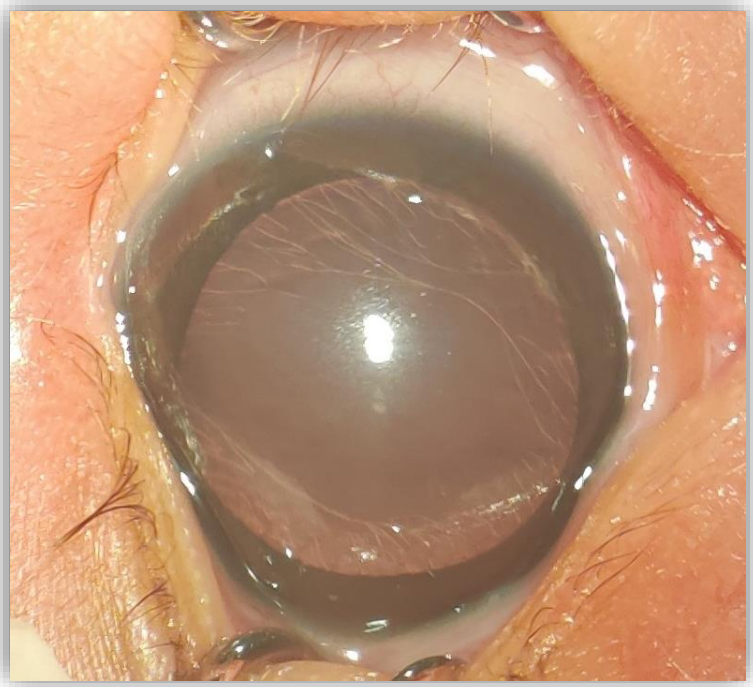
COMMENTS:
EXAMINING DOCTOR: **SIGNATURE**

ANNEXURE-IV

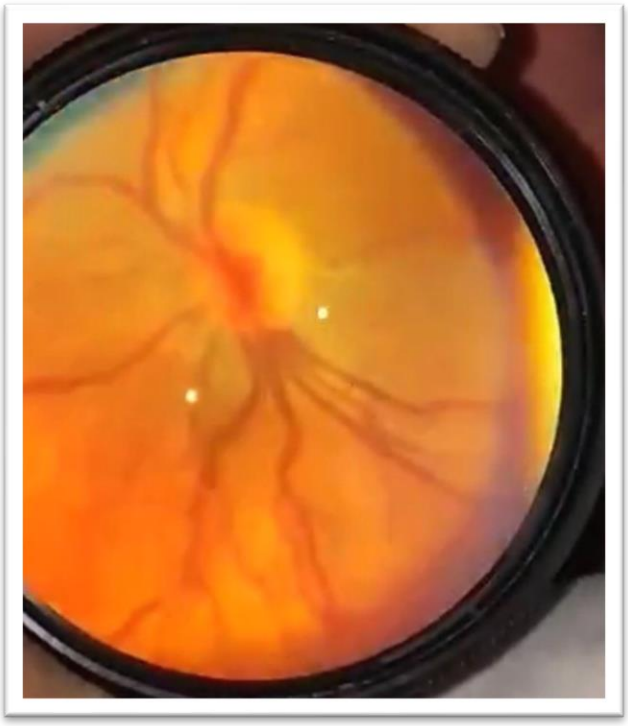
Photograph 2: ROP screening being performed in the NICU



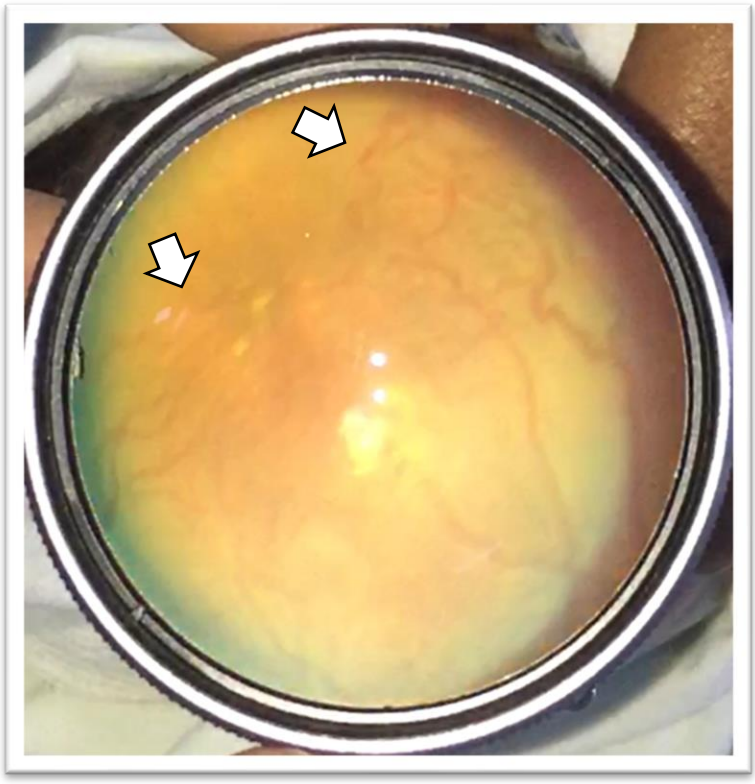
Photograph 3: Instruments used for ROP screening



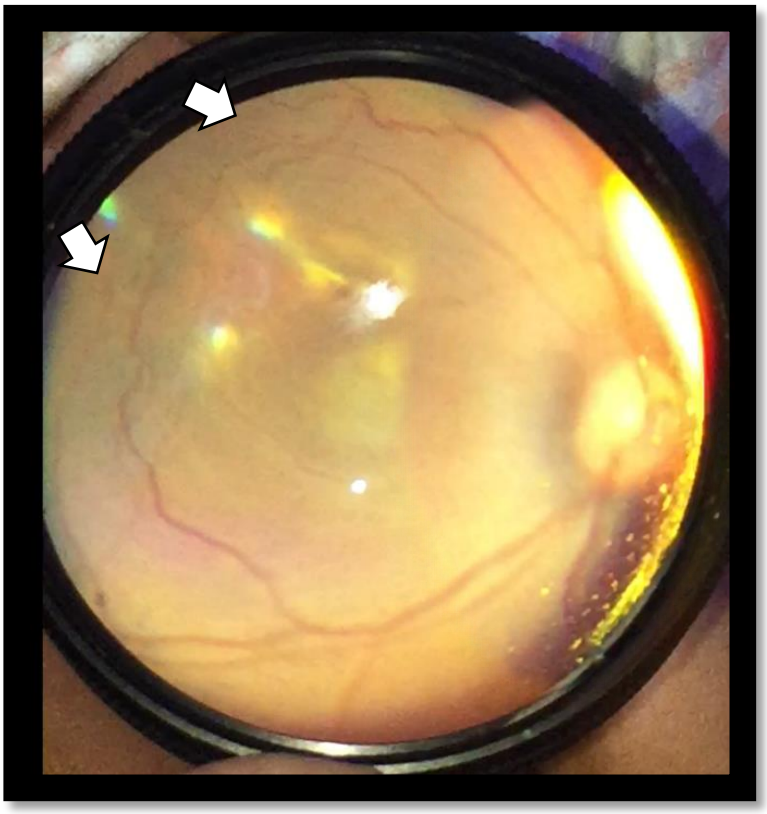
Photograph 4: Tunica Vasculosa lentis



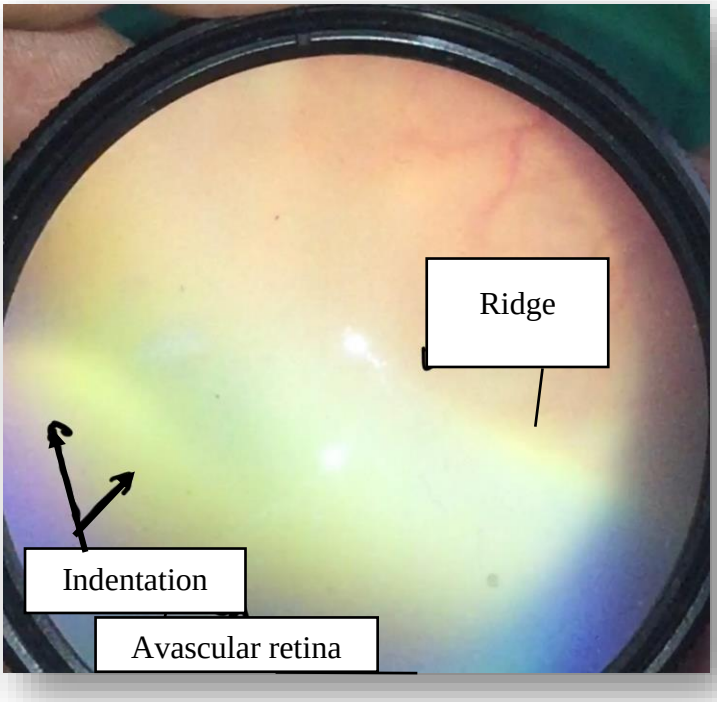
Photograph 5: Plus disease



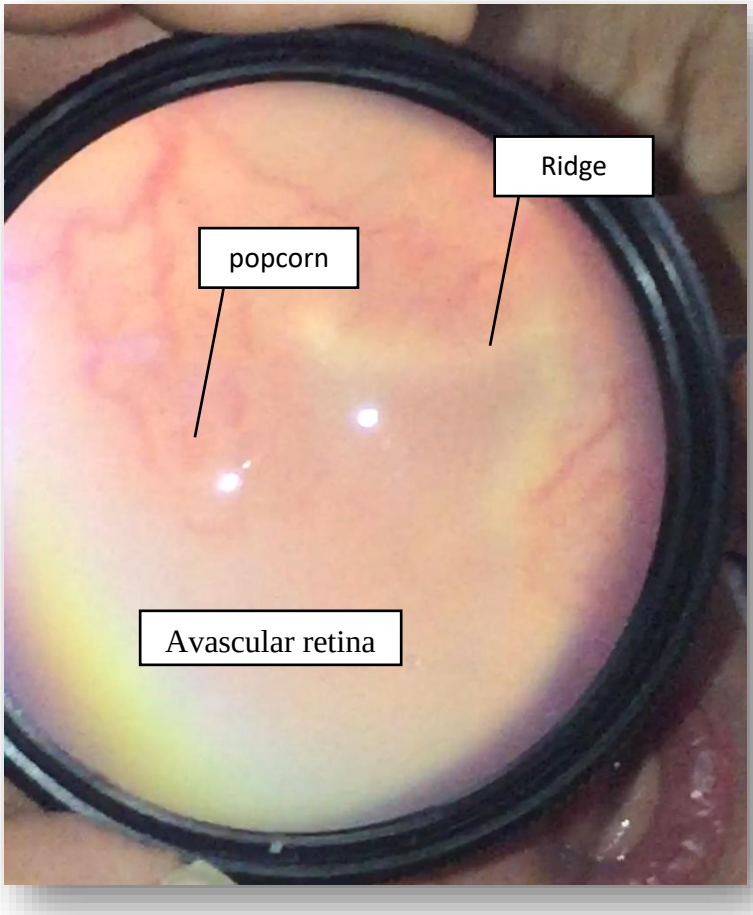
Photograph 6: Communicating vessels, APROP



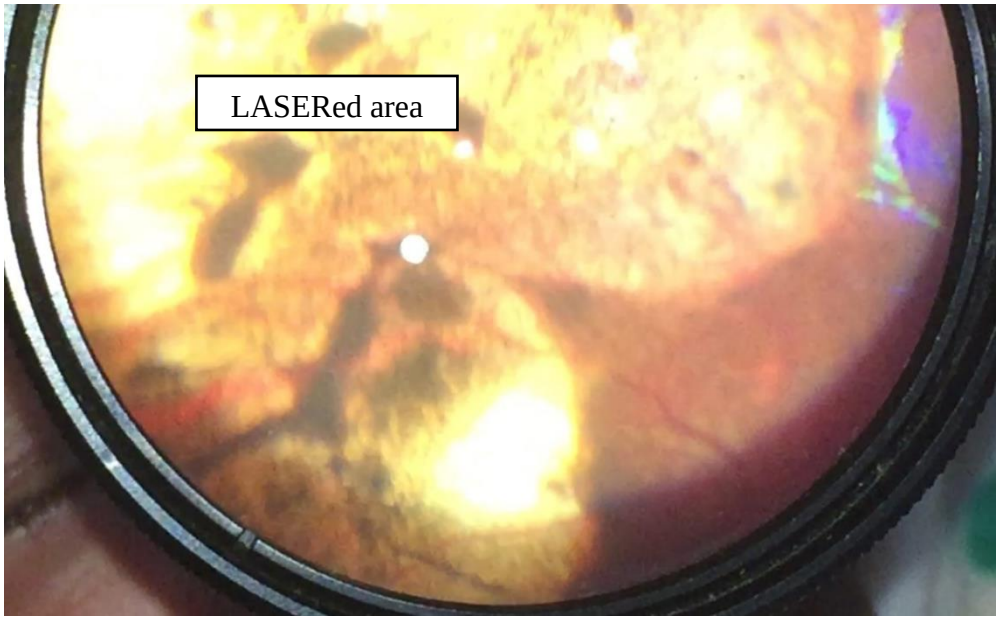
Photograph 7: Fundus image showing Demarcation line and avascular retina



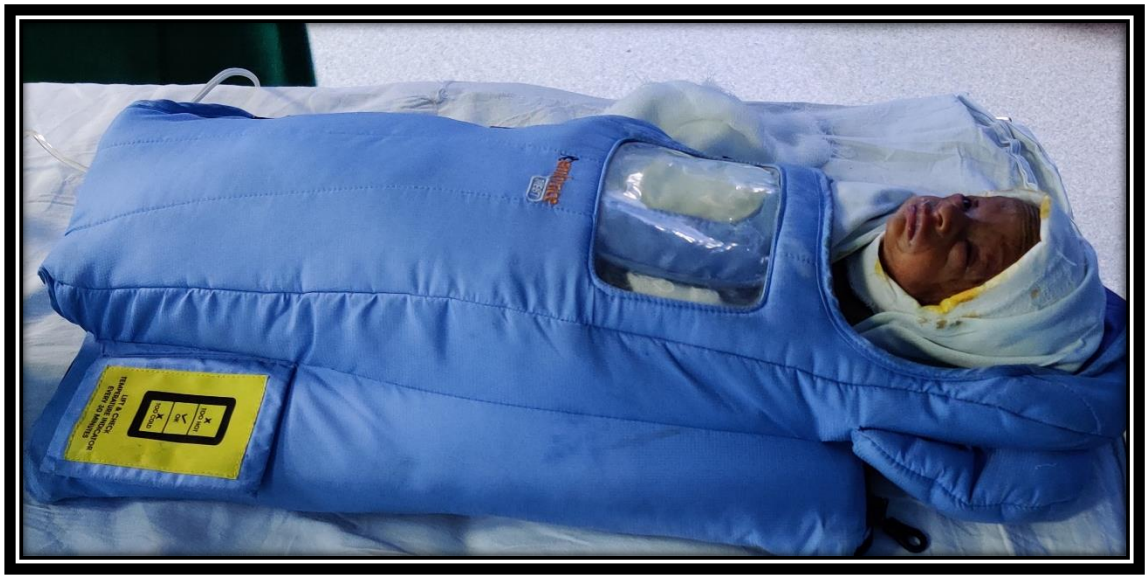
Photograph 8: Ridge, avascular retina, and indentation



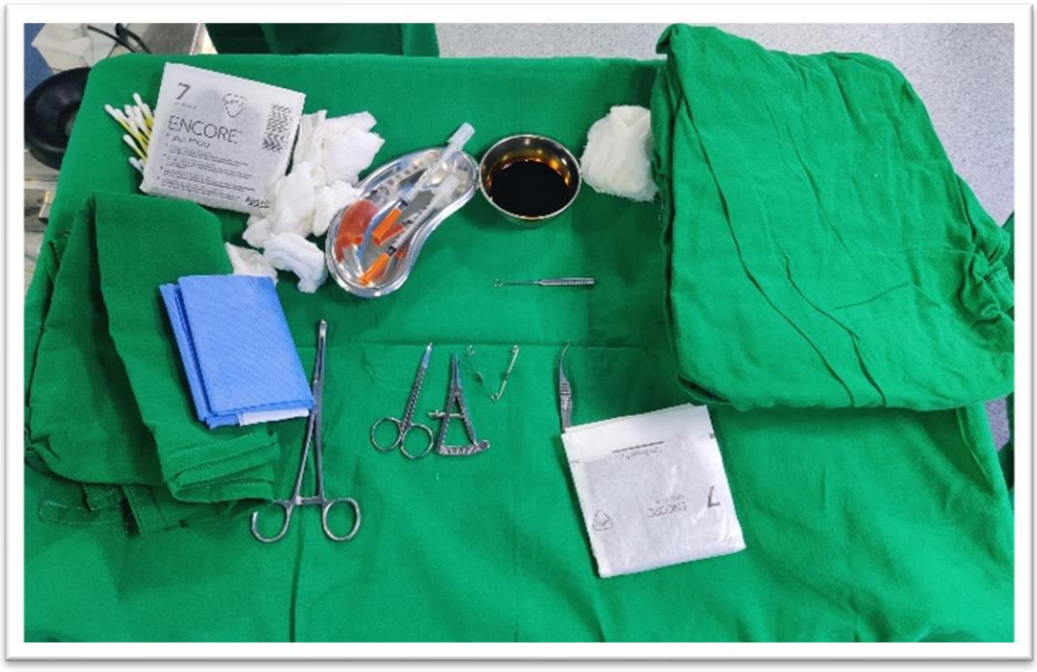
Photograph 9: Stage 2 ROP with Islands of avascular retina in-between areas of vascularized retina



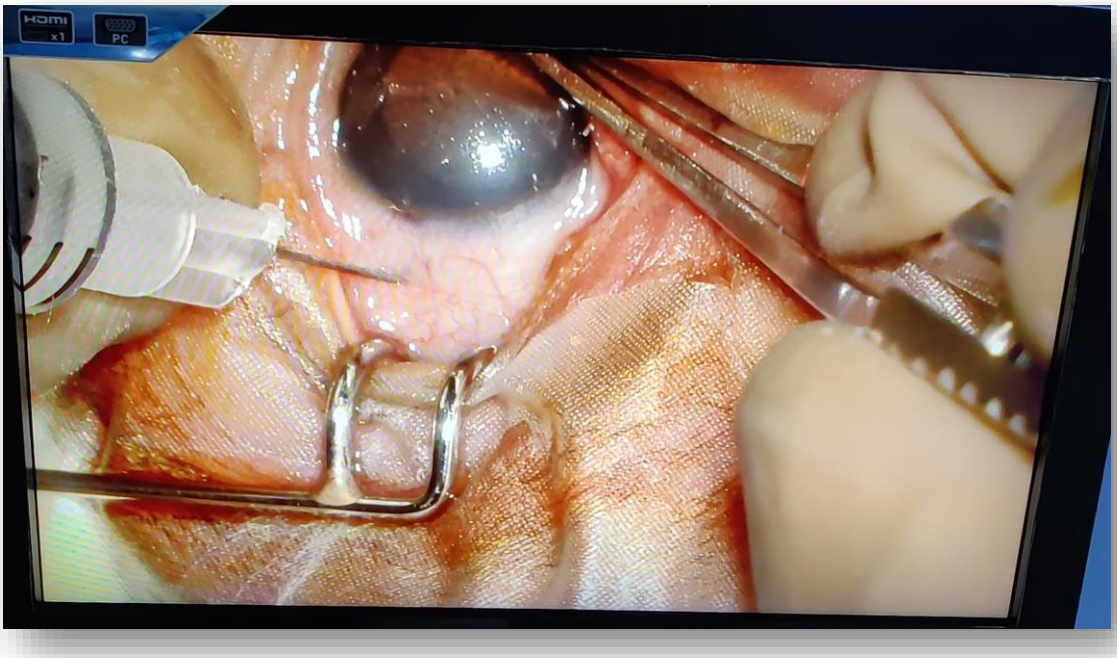
Photograph 10: Post laser scar in the avascular retina



Photograph 11: An Infant wrapped in an Embrace nest baby warmer

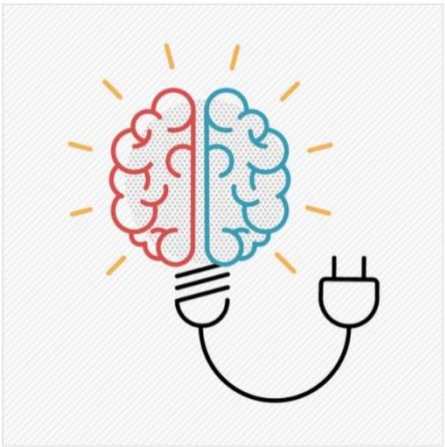


Photograph 12: OT trolley preparation for intravitreal anti-VEGF injection



Photograph 13: Intravitreal injection being given

Photograph 14: LASER being delivered in the presence of a paediatrician



ANNEXURE-V

KEY TO MASTERCHART

No. : Infant number

GA : Gestational age at birth (weeks)

BW : Birth weight (grams)

GENDER : Gender

M = Male F= Female

PARITY : Parity

1 = Singleton

2 = twins

3 = triplets

STEROIDS : Prenatal steroids

0 = not administered

1 = 1 dose administered

2 = 2 doses administered

MOD : Mode of delivery

N = Normal vaginal delivery

F = Forceps

C = Lower segment Caeserian Section

VA = Vacuum

GDM : Gestational Diabetes

N = no Diabetes

Y = Gestational Diabetes Mellitus

MHTN : Maternal Hypertension

N = absent

Y = present

PPROM : Preterm premature rupture of membranes

N = absent

Y = present

OMF : Other maternal factors

0 = Absent

1 = Oligohydramnios

2 = Hypothyroidism

3 = Antepartum hemorrhage

4 = Excess liquor

5 = Lupus nephritis

6 = Placenta previa

7 = Epilepsy

8 = Rheumatic heart disease

9 = HSV 1 & 2

10 = Rh -ve pregnancy

11 = Toxoplasma

12 = Abruptio-placenta

13 = HELLP syndrome

14 = Latent labour

RDS : Respiratory Distress syndrome

N = absent

Y = present

AOP : Apnoea of prematurity

N = absent

Y = present

ASPHYXIA : Perinatal asphyxia

N = absent

Y = present

PDA : Patent Ductus arteriosus

N = absent

Y = present

PDAT : PDA treatment

0 = no treatment given

1 = medical management

2 = surgical management

SEPSIS : Sepsis

0 = no sepsis

1 = Fungal sepsis

2 = Bacterial sepsis

3 = Bacterial + Fungal sepsis

IVH : Intraventricular Hemorrhage

N = absent

Y = present

ANEMIA : Anaemia

N = absent

Y = present

NNS : Neonatal seizures

N = absent

Y = present

SURFACT : Surfactant

N = absent

Y = present

B&M : Bag and mask resuscitation

N = absent

Y = present

PMA : Mechanical ventilation in number of days

O2 : Oxygen supplementation in number of days

BLOOD : Blood product transfusion

0 = not given

1 = up to 5 transfusions

2 = more than 5 transfusions

FFP : Fresh frozen plasma in number of units transfused

PL : Platelets in number of units transfused

PC : Packed cells in number of units transfused

RE ZONE : Right eye Zone

I = Zone I

II = Zone II

III = Zone III

RE STAGE : Right eye Stage of ROP

1 = Stage 1

2 = Stage 2

3 = Stage 3

4a = Stage 4A

4b = Stage 4B

5 = Stage 5

RE PLUS : Right eye Plus disease

Y = present

N = absent

LE ZONE : Left eye Zone

I = Zone I

II = Zone II

III = Zone III

LE STAGE : Left eye Stage of ROP

1 = Stage 1

2 = Stage 2

3 = Stage 3

4a = Stage 4A

4b = Stage 4B

5 = Stage 5

LE PLUS : Left eye Plus disease

Y = present

N = absent

ANY ROP : Any stage of Retinopathy of Prematurity

N = absent

Y = present

TYPE 1 ROP : Type 1 Retinopathy of prematurity

N = absent

Y = present

PCA D : minimum post-conception age at which any stage of ROP was first detected (weeks)

PCA T : Post conceptional age at treatment (weeks)

TREAT : Treatment

O = Observation

L = Laser

I = Intravitreal injection

B = Intravitreal injection followed by laser

RE TREAT : Relaser

N = absent

Y = present

ANNEXURE-VI

No.	GA	BW	GENDER	PARITY	STEROIDS	MOD	GDM	MHTN	PPROM	OMF	RDS	AOP	ASPHYXIA	PDA	PDAT	SEPSIS	IVH	ANEMIA	NNS	SURFACT	BR M	PMA	O2	BLOOD	FFP	PLATELET	PACKED CELL	RE ZONE	RE STAGE	RE PLUS	LE ZONE	LE STAGE	LE PLUS	ANY ROP	TYPE I ROP	PCA D	PCA T	TREAT	RE TREAT
101	34	1670	M	1	2	V	N	N	N	1	Y	N	N	N	0	1	N	N	N	N	N	0	2	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
102	29	1440	F	2	2	C	N	Y	Y	0	Y	Y	N	Y	0	3	N	Y	N	N	N	6	2	1	0	0	0	II	0	N	II	0	N	Y	N	35	0	O	N
103	29	1440	F	2	2	C	N	Y	N	0	Y	N	N	N	1	3	N	N	N	N	N	5	3	0	0	0	0	II	0	N	II	0	N	N	N	35	0	O	N
104	35	1450	M	1	0	C	N	Y	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
105	32	1520	M	1	0	C	N	Y	N	2	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	Y	III	0	N	Y	N	0	0	O	N
106	34	2200	M	1	0	C	N	Y	N	3	Y	N	N	N	0	0	N	Y	Y	N	Y	5	11	1	0	2	2	III	2	N	III	2	N	Y	N	40	0	O	N
107	34	2760	M	1	2	C	Y	Y	N	0	Y	N	N	N	0	0	N	N	N	N	Y	0	3	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
108	32	1800	M	1	0	C	N	N	N	4	Y	N	N	N	0	2	N	N	N	N	N	0	0	1	0	2	0	III	0	N	III	0	N	N	N	0	0	O	N
109	32	1640	F	1	0	V	N	N	Y	4	N	Y	N	Y	1	3	N	Y	N	N	N	6	16	1	0	5	0	III	0	N	III	0	N	N	N	0	0	O	N
110	35	2500	M	1	0	V	N	N	N	4	N	Y	N	N	0	3	N	N	N	N	N	6	14	1	0	0	2	M	0	N	M	0	N	N	N	0	0	O	N
111	34	1500	F	1	0	C	Y	Y	N	2,4	N	Y	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	II	0	N	N	N	0	0	O	N
112	34	1600	F	1	2	C	N	Y	N	1,2	N	Y	N	N	0	0	N	N	N	N	N	3	0	0	0	0	0	M	0	N	III	0	N	N	N	0	0	O	N
113	33	1580	M	1	0	C	N	N	N	0	Y	Y	N	N	0	0	N	N	N	N	Y	6	0	0	0	0	0	M	0	N	III	1	N	Y	N	37	0	O	N
114	34	1550	M	1	0	C	N	N	N	0	N	N	N	N	0	1	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
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117	34	1540	F	2	0	C	N	N	N	0	Y	Y	N	Y	0	1	N	N	N	N	N	2	8	1	0	2	0	III	0	N	III	0	N	N	N	0	0	O	N
118	35	1350	M	1	0	C	N	N	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
119	29	1500	M	1	1	V	N	N	N	0	Y	N	N	N	0	1	N	N	N	N	N	0	3	1	0	2	0	II	0	N	II	0	N	N	N	0	0	O	N
201	32	1800	M	1	0	V	N	N	Y	2	N	N	N	N	0	1	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
202	34	1600	F	1	0	C	N	Y	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
203	34	1200	M	2	0	C	N	Y	N	0	N	N	N	N	0	0	N	N	N	N	Y	0	0	1	0	1	0	III	0	N	II	0	N	N	N	0	0	O	N
204	34	1500	F	1	0	C	N	Y	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
205	32	1700	M	1	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	3	1	0	2	0	II	0	N	II	0	N	Y	N	39	0	O	N
206	28	1040	M	2	0	C	N	N	N	0	Y	N	N	N	0	1	N	Y	N	N	Y	0	10	1	3	0	0	II	0	N	II	0	N	Y	Y	28	33	L	Y
207	34	2060	F	2	0	C	Y	Y	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	II	0	N	N	N	0	0	O	N
208	34	1870	M	2	0	C	Y	Y	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
209	34	2300	M	1	0	C	N	N	Y	0	Y	N	N	N	0	0	N	N	N	N	N	4	5	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
210	29	1270	M	3	0	C	N	N	Y	0	Y	N	N	N	0	0	N	N	N	N	N	2	6	0	0	0	0	II	2	N	II	2	N	Y	N	34	0	O	N
211	34	1810	F	1	0	V	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
212	37	1510	M	1	0	C	N	Y	N	5	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	M	0	N	N	N	0	0	O	N
213	35	1510	F	2	0	C	N	Y	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
214	35	2000	F	2	0	C	N	Y	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N

No.	GA	BW	GENDER	PARITY	STEROIDS	MOD	GDM	MHTN	PPROM	OMF	RDS	AOP	ASPHYXIA	PDA	PDAT	SEPSIS	IVH	ANEMIA	NNS	SURFACT	Bk. M	PMA	O2	BLOOD	EFP	PLATELET	PACKED CELL	RE ZONE	RE STAGE	RE PLUS	LE ZONE	LE STAGE	LE PLUS	ANY ROP	TYPE I ROP	PCA D	PCA T	TREAT	RE TREAT
215	28	960	F	2	2	C	N	Y	N	0	Y	N	N	Y	0	1	N	N	N	N	N	2	6	0	0	3	0	III	2	Y	II	2	N	Y	Y	28	28	L	Y
216	28	716	M	2	2	C	N	Y	N	0	Y	N	N	Y	0	1	N	N	N	N	N	0	8	1	0	2	0	II	2	N	II	2	N	N	Y	28	35	L	N
217	31	1150	M	1	0	V	N	N	N	0	Y	N	Y	N	0	2	N	N	N	N	Y	0	4	0	0	5	0	III	0	N	III	0	N	N	N	38	38	O	N
218	38	1480	F	1	0	V	N	N	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	4	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
301	31	1400	M	1	2	V	N	N	Y	0	N	N	N	N	0	0	N	N	N	N	N	0	0	1	0	2	0	II	0	N	II	0	N	N	N	0	0	O	N
302	35	2250	F	2	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
303	35	1800	F	2	0	C	N	N	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
304	32	1600	F	1	0	V	N	N	N	0	N	Y	Y	N	1	0	N	N	N	N	N	0	1	0	0	0	0	M	0	N	M	0	N	N	Y	47	0	O	N
305	33	1250	M	1	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	2	0	0	0	0	III	0	N	III	2	N	N	N	0	0	O	N
306	35	1660	M	1	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
307	31	1640	F	1	2	C	N	Y	N	0	N	N	N	N	0	1	N	Y	N	N	N	0	2	1	1	2	0	III	2	N	III	2	N	N	N	0	0	O	N
308	34	1700	F	1	2	C	N	Y	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
309	31	1000	M	1	0	C	Y	Y	N	6	N	Y	N	N	0	2	N	Y	N	N	N	1	7	1	0	2	2	II	0	N	II	0	N	N	N	0	0	L	N
310	32	1700	M	2	0	C	Y	Y	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	Y	39	0	O	N
311	32	1700	M	2	0	C	Y	Y	N	0	N	Y	N	N	0	2	N	N	N	N	N	1	3	1	0	2	0	III	0	N	III	0	N	N	N	0	0	O	N
312	34	1600	F	0	2	C	N	N	N	0	N	Y	Y	N	0	0	N	N	N	Y	N	0	0	0	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
313	31	2100	M	1	0	C	Y	Y	N	7	N	N	Y	N	0	0	N	N	N	Y	N	1	2	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
314	31	1060	F	1	2	C	N	Y	N	0	Y	N	N	N	0	0	N	Y	N	N	N	0	3	1	0	4	0	III	0	N	II	0	N	N	Y	38	0	O	N
315	34	1600	F	2	0	C	Y	N	N	0	N	N	N	Y	0	0	N	N	N	N	N	0	0	0	0	0	0	II	0	N	II	0	N	N	Y	39	0	O	N
316	34	2300	F	2	4	C	Y	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	3	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
317	32	1440	F	1	0	C	N	N	N	0	Y	N	N	N	0	1	N	N	N	N	N	0	8	0	0	0	0	II	0	N	II	0	N	N	N	36	0	O	N
318	34	1300	F	1	0	C	N	Y	N	0	N	N	Y	N	0	1	N	N	N	N	N	0	2	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
319	32	1700	M	1	0	V	N	N	N	0	Y	Y	N	Y	0	1	N	N	N	N	N	0	0	0	0	0	0	II	0	N	II	0	N	N	N	36	0	O	N
320	35	2130	M	1	0	V	N	N	N	0	N	N	N	Y	0	1	N	Y	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	40	0	O	N
321	35	1640	F	2	0	C	N	N	N	0	N	N	N	N	0	1	N	N	N	N	N	2	1	1	4	0	0	III	0	N	III	0	N	N	N	0	0	O	N
322	35	1940	F	2	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	3	2	5	4	0	III	0	N	III	0	N	N	N	0	0	O	N
323	33	1100	M	1	0	C	Y	Y	N	0	N	N	N	N	0	1	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
401	32	1300	M	1	0	C	N	Y	N	0	N	N	N	N	0	1	N	N	N	N	N	0	2	1	0	2	0	III	1	N	III	1	N	Y	N	38	0	O	N
402	33	1700	M	1	0	C	N	N	Y	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	II	0	N	II	0	N	N	N	34	0	O	N
403	36	1700	M	1	0	V	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	II	0	N	N	N	0	0	O	N
404	31	1400	F	2	0	C	N	Y	N	0	Y	N	N	N	0	1	N	N	N	N	N	2	6	1	0	2	1	III	0	N	III	0	N	N	N	0	0	O	N
405	38	1920	F	1	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	44	0	O	N
406	34	1600	F	1	0	C	Y	Y	N	0	Y	N	N	N	0	1	N	N	N	N	N	0	1	2	4	6	0	II	0	N	II	0	N	N	N	0	0	O	N
407	39	2600	M	1	0	C	N	N	N	8	Y	N	N	N	0	1	N	N	N	N	N	0	4	2	2	14	0	III	0	N	III	0	N	N	N	0	0	O	N

No.	GA	BW	GENDER	PARITY	STEROIDS	MOD	GDM	MHTN	PPROM	OMF	RDS	AOP	ASPHYXIA	PDA	PDAT	SEPSIS	IVH	ANEMIA	NNS	SURFACT	B& M	PMA	O2	BLOOD	EFP	PLATELET	PACKED CELL	RE ZONE	RE STAGE	RE PLUS	LE ZONE	LE STAGE	LE PLUS	ANY ROP	TYPE I ROP	PCA D	PCA T	TREAT	RE TREAT
408	35	1940	F	2	0	C	N	N	N	0	Y	N	N	N	0	2	N	Y	N	N	N	0	3	2	6	7	0	III	0	N	III	0	N	N	N	0	0	O	N
409	35	1840	F	2	0	C	N	Y	N	0	Y	N	N	N	0	1	N	N	N	N	N	2	0	1	0	4	0	III	1	N	III	0	N	N	N	0	0	O	N
410	32	1200	F	1	0	C	N	Y	N	0	Y	N	N	N	0	2	N	Y	N	N	N	3	5	2	0	6	0	III	0	N	III	0	N	N	N	0	0	O	N
411	31	1480	F	1	0	C	N	N	N	0	N	N	N	N	0	1	N	N	N	N	N	0	0	0	0	2	0	II	0	N	II	0	N	N	N	0	0	O	N
412	27	910	F	1	0	C	N	N	N	0	Y	Y	N	N	0	1	N	N	N	N	Y	3	12	1	0	2	0	II	2	N	III	2	N	N	N	0	0	O	N
413	32	1180	M	1	0	V	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	2	0	M	0	N	M	0	N	N	N	0	0	O	N
414	30	1400	M	1	0	C	N	Y	N	2	N	N	Y	N	0	0	N	N	N	N	Y	4	8	0	0	0	0	II	0	N	II	0	N	N	Y	0	34	O	N
415	33	1300	F	1	0	V	N	N	N	0	Y	Y	N	N	0	1	N	N	N	N	N	0	1	0	0	0	0	II	0	N	II	0	N	N	Y	0	35	O	N
416	30	1300	M	1	2	C	N	N	N	0	Y	N	N	N	0	0	N	N	N	N	N	5	4	0	0	0	0	III	1	N	III	0	N	N	N	0	0	O	N
417	35	1800	M	1	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
418	33	1630	F	1	0	C	N	N	N	0	Y	N	N	N	0	1	N	N	N	N	N	2	8	0	0	0	0	III	2	N	III	0	N	N	Y	0	37	O	N
419	32	1800	F	1	0	C	N	Y	N	0	Y	N	N	N	0	1	N	N	N	N	N	3	5	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
420	31	1070	F	1	2	C	N	Y	N	0	Y	N	N	N	0	0	N	Y	N	N	N	0	3	1	0	4	0	III	0	N	III	0	N	N	N	0	0	O	N
421	40	1910	F	1	0	V	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
422	31	1350	F	1	0	C	N	Y	N	0	Y	Y	N	N	0	0	N	N	N	N	N	1	3	0	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
423	35	1580	F	1	0	C	N	N	N	0	Y	N	N	N	0	1	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
424	39	1900	F	1	0	V	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
425	32	1080	F	1	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
426	32	1860	M	1	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
427	32	1950	M	2	2	C	N	N	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
428	32	1980	M	2	2	C	N	N	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
429	33	1920	M	1	2	C	N	Y	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	Y	0	40	O	N
430	36	2000	M	1	0	C	N	N	N	0	N	N	N	N	0	0	N	Y	N	N	N	0	0	0	0	1	0	III	0	N	III	0	N	N	N	0	0	O	N
431	35	1410	F	1	0	C	N	N	N	0	Y	Y	N	N	0	1	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
432	33	1790	F	1	0	C	N	N	N	0	Y	N	Y	N	0	1	N	Y	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
501	36	2400	M	1	0	C	N	N	N	0	Y	N	N	N	0	1	N	Y	N	N	N	0	0	0	0	3	0	III	0	N	III	0	N	N	N	0	0	O	N
502	32	1500	F	2	2	C	N	N	N	0	Y	N	N	N	0	1	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
503	32	1800	M	2	2	C	N	N	N	0	Y	N	N	N	0	1	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
504	33	1000	M	1	0	C	N	Y	N	0	N	Y	N	N	0	0	N	N	N	N	Y	1	2	0	0	0	0	II	3	Y	II	2	Y	Y	Y	35	L	O	N
505	29	1080	F	2	0	C	N	N	Y	0	Y	Y	N	Y	0	1	N	Y	N	N	Y	3	15	2	5	5	1	II	0	N	II	0	N	Y	N	33	O	O	N
506	30	1200	F	1	0	C	N	Y	N	0	N	Y	N	N	0	2	N	Y	N	N	Y	0	0	2	0	6	1	II	0	Y	II	0	N	Y	Y	34	L	O	N
507	29	845	F	1	0	C	N	Y	N	0	Y	N	Y	N	0	2	N	Y	N	N	Y	3	3	1	0	4	0	II	1	N	II	0	N	Y	N	32	O	O	N
508	32	1660	M	1	0	C	Y	Y	N	2	N	N	N	N	0	0	N	N	N	N	N	0	1	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
509	32	1720	M	2	0	C	Y	Y	N	2	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N

No.	GA	BW	GENDER	PARITY	STEROIDS	MOD	GDM	MHTN	PPROM	OMF	RDS	AOP	ASPHYXIA	PDA	PDAT	SEPSIS	IVH	ANEMIA	NNS	SURFACT	B& M	PMA	O2	BLOOD	FFP	PLATELET	PACKED CELL	RE ZONE	RE STAGE	RE PLUS	LE ZONE	LE STAGE	LE PLUS	ANY ROP	TYPE I ROP	PCA D	PCA T	TREAT	RE TREAT
510	34	1500	M	1	1	C	N	Y	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	M	0	N	N	N	0	0	O	N
511	35	2200	M	2	0	C	N	N	N	0	Y	Y	N	N	0	1	N	N	N	N	N	0	3	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
512	29	970	F	1	0	V	N	Y	N	0	Y	N	N	Y	0	3	N	Y	N	Y	N	0	27	1	0	0	1	II	0	N	II	0	N	N	N	0	0	O	N
513	33	1400	M	1	0	C	N	N	N	0	N	N	N	N	0	1	N	N	N	N	N	1	3	1	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
514	33	1680	M	1	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
515	34	1600	M	1	1	C	N	Y	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	17	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
516	34	1500	M	1	0	C	N	N	N	0	Y	N	N	N	0	0	N	N	N	Y	N	0	3	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
517	36	1760	M	1	1	C	N	Y	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
518	35	1820	F	1	0	C	N	N	Y	0	N	Y	N	N	0	1	N	N	N	N	N	0	4	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
519	35	1420	M	2	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
520	35	2000	M	2	0	C	N	N	N	0	Y	Y	N	N	0	0	N	N	N	N	N	1	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
521	32	1200	M	1	0	C	N	N	N	0	Y	Y	N	N	0	1	N	Y	N	N	N	0	1	0	0	0	1	III	0	N	III	0	N	N	N	0	0	O	N
522	30	1500	M	1	0	C	N	N	N	2	Y	Y	N	N	0	2	N	N	N	N	N	0	8	1	1	3	0	II	0	N	II	0	N	N	N	35	0	L	N
523	35	1300	M	1	0	C	N	N	N	0	Y	N	N	N	0	1	N	N	N	Y	N	0	0	0	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
524	33	1820	F	1	0	C	N	N	N	0	N	Y	N	N	0	1	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
525	36	2400	M	1	0	C	N	N	N	0	N	N	N	Y	0	1	N	N	N	N	N	0	4	0	0	0	0	III	0	N	M	0	N	N	N	0	0	O	N
601	40	2640	M	1	0	V	N	N	N	0	Y	N	N	N	0	1	N	N	N	N	N	0	4	1	3	2	0	II	0	N	II	0	N	M	N	32	0	O	N
602	29	840	F	1	0	C	N	Y	N	0	Y	N	N	N	0	2	N	N	N	N	N	0	5	1	0	4	0	II	0	N	II	0	N	N	Y	N	0	O	N
603	32	1400	M	1	0	C	N	Y	N	0	Y	N	N	N	0	3	N	Y	N	N	N	11	13	2	7	8	1	II	0	N	II	0	N	N	N	0	0	O	N
604	34	2200	M	1	0	C	N	Y	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
605	39	2600	M	1	0	C	N	N	N	0	N	N	N	N	0	1	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	51	0	O	N
606	31	1440	M	1	0	V	N	N	N	0	N	N	Y	N	0	1	N	Y	N	Y	N	0	8	2	3	3	1	III	0	N	III	0	N	N	N	0	0	O	N
607	36	1700	F	1	0	C	N	Y	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
608	34	1430	F	1	1	V	N	Y	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	1	0	0	0	0	II	0	N	II	0	N	N	Y	0	0	O	N
609	31	1350	M	1	0	C	N	Y	N	13	Y	N	N	N	1	1	N	N	N	Y	N	1	3	0	0	0	0	II	0	Y	II	0	N	N	Y	34	0	O	N
610	34	1400	M	2	1	C	N	N	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
611	34	1960	F	2	1	C	N	N	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	1	0	0	0	0	M	0	N	M	0	N	N	Y	33	0	O	N
612	27	952	M	1	0	C	N	N	Y	2	Y	N	N	N	0	1	N	N	N	N	N	2	24	1	0	1	1	II	0	N	II	0	N	N	Y	0	0	O	N
613	31	1440	M	1	0	V	N	N	N	0	Y	N	N	Y	0	1	N	N	N	Y	N	1	4	0	0	0	0	M	0	N	M	0	N	N	Y	0	0	O	N
614	36	2600	F	1	0	C	N	N	N	0	N	Y	Y	Y	1	1	N	N	N	N	N	0	7	2	0	4	2	III	0	N	III	2	N	N	Y	40	0	O	N
615	26	800	F	1	0	V	N	N	N	0	N	Y	N	N	0	1	N	N	N	N	N	15	17	1	0	2	1	II	0	N	II	0	N	N	Y	38	0	O	N
616	32	1160	F	1	2	C	N	N	Y	0	N	N	N	N	0	1	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
617	29	970	F	1	2	V	N	Y	N	0	Y	N	Y	Y	1	1	N	N	N	N	N	1	5	2	0	4	4	III	2	N	III	2	N	N	Y	37	0	O	N
618	33	1700	M	1	0	V	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N

No.	GA	BW	GENDER	PARITY	STEROIDS	MOD	GDM	MHTN	PPROM	OMF	RDS	AOP	ASPHYXIA	PDA	PDAT	SEPSIS	IVH	ANEMIA	NNS	SUREFACT	Bk M	PMA	O2	BLOOD	FFP	PLATELET	PACKED CELL	RE ZONE	RE STAGE	RE PLUS	LE ZONE	LE STAGE	LE PLUS	ANY ROP	TYPE I ROP	PCA D	PCA T	TREAT	RE TREAT
619	36	1980	M	2	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
620	36	1800	M	2	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
621	31	1300	M	1	0	C	N	N	N	0	Y	N	N	N	0	3	N	N	N	N	N	0	0	1	0	1	0	II	0	N	III	0	N	N	N	0	0	O	N
622	37	1670	F	2	0	C	N	N	Y	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
623	36	2170	M	2	0	C	N	N	Y	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	2	N	M	0	N	N	N	0	0	O	N
701	35	1900	F	1	0	C	N	Y	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	1	0	0	3	0	III	0	N	M	0	N	N	N	0	0	O	N
702	37	1500	M	2	2	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
703	38	1900	F	1	0	V	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	10	0	M	0	N	M	0	N	N	N	0	0	O	N
704	34	1900	M	1	0	C	N	Y	N	14	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
705	36	1700	F	1	0	C	N	Y	N	2	Y	N	N	Y	0	2	Y	N	N	N	N	0	6	0	0	1	1	III	0	N	II	0	N	N	N	0	0	O	N
706	34	1930	F	2	0	C	N	N	N	0	N	N	N	N	0	0	Y	N	N	N	N	0	0	0	0	0	1	II	0	N	II	0	N	N	N	0	0	O	N
707	34	1700	F	2	0	C	N	N	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	II	0	N	N	N	0	0	O	N
708	32	1200	F	1	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	2	Y	III	2	N	N	N	37	0	O	N
709	36	1400	F	1	0	C	N	Y	N	0	N	N	N	N	0	1	N	N	N	N	N	0	2	1	0	3	0	III	0	N	III	0	N	N	N	0	0	O	N
710	36	1900	M	1	0	C	N	Y	N	2	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
711	33	1840	M	1	2	C	N	N	N	0	Y	N	N	Y	0	0	N	N	N	N	N	3	5	0	0	0	0	III	2	N	III	2	N	Y	N	39	0	O	N
712	31	1200	M	2	0	C	N	N	N	0	Y	N	N	N	0	2	N	Y	N	N	N	0	1	0	0	2	1	II	1	N	II	0	N	Y	N	36	0	O	N
713	31	1400	M	2	0	C	N	N	N	0	Y	N	N	N	0	2	N	N	N	N	N	0	1	0	0	2	0	M	0	N	M	0	N	N	N	0	0	O	N
714	33	1370	F	1	0	V	N	N	N	0	Y	N	N	N	0	1	N	N	N	N	N	1	5	2	0	10	0	III	2	N	III	2	N	Y	N	37	0	O	N
715	32	1400	M	1	0	C	N	Y	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
716	30	1670	M	1	2	C	N	N	Y	0	Y	N	N	N	0	0	N	N	N	N	Y	8	23	0	0	0	0	II	0	N	II	0	N	Y	N	34	0	L	N
717	35	2800	M	1	1	V	N	N	N	0	Y	N	N	N	0	0	N	N	N	N	N	2	1	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
718	33	2000	M	2	2	C	N	Y	N	0	Y	N	N	N	0	1	N	N	N	N	N	0	6	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
719	33	1500	M	2	2	C	N	Y	N	0	Y	N	N	N	0	1	N	N	N	N	N	0	5	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
720	36	1900	M	1	0	V	N	N	N	10	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
721	36	1700	M	1	0	VA	N	N	Y	9	N	N	N	N	0	0	N	N	N	N	N	0	3	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
722	34	1600	F	1	0	C	N	Y	N	3	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
723	35	1700	M	1	0	V	N	N	N	3	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
724	31	1700	M	1	0	C	N	Y	N	0	Y	N	N	N	0	1	N	N	N	N	N	1	6	0	0	0	0	II	0	N	II	0	N	Y	N	39	0	O	N
801	35	2240	F	1	0	C	N	Y	N	0	Y	N	N	N	0	0	N	N	N	N	N	1	2	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
802	30	976	F	1	2	C	Y	Y	N	0	N	N	N	N	0	1	N	N	N	N	N	0	3	1	0	1	0	II	0	N	II	0	N	Y	N	0	0	O	N
803	32	1500	M	1	2	V	Y	N	N	10	Y	N	N	N	0	1	N	N	N	N	N	2	14	1	0	5	0	III	0	N	II	0	N	N	N	0	0	O	N
804	34	1970	F	2	0	V	N	Y	N	2	Y	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
805	34	1680	M	2	0	V	N	Y	N	2	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N

No.	GA	BW	GENDER	PARITY	STEROIDS	MOD	GDM	MHTN	PPROM	OMF	RDS	AOP	ASPHYXIA	PDA	PDAT	SEPSIS	IVH	ANEMIA	NNS	SURFACT	B& M	PMA	O2	BLOOD	EFP	PLATELET	PACKED CELL	RE ZONE	RE STAGE	RE PLUS	LE ZONE	LE STAGE	LE PLUS	ANY ROP	TYPE I ROP	PCA D	PCA T	TREAT	RE TREAT
806	31	1390	F	1	0	V	N	N	N	0	N	Y	N	Y	1	1	N	N	N	N	N	0	1	0	0	0	0	II	0	N	II	0	N	N	0	0	O	N
807	35	1900	M	1	0	V	N	N	N	1	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	0	0	O	N
808	37	2400	M	1	0	V	N	Y	N	0	Y	Y	N	N	0	0	N	N	N	N	N	4	4	0	0	0	0	III	0	N	III	0	N	N	0	0	O	N
809	35	1830	M	1	0	C	N	Y	N	15	N	N	N	N	0	0	N	N	N	N	N	0	5	0	0	0	0	III	0	N	III	0	N	N	0	0	O	N
810	35	1600	F	2	0	C	N	Y	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	0	0	O	N
811	35	1900	M	2	0	C	N	Y	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	0	0	O	N
812	39	966	F	2	0	C	N	N	N	0	Y	Y	N	Y	0	3	N	Y	N	N	Y	18	23	2	0	8	0	II	0	N	II	0	N	N	0	35	O	N
813	30	1240	F	1	0	V	N	N	N	0	Y	Y	N	N	0	2	N	N	N	N	N	0	0	0	0	0	0	II	0	N	II	0	N	Y	N	37	I	N
814	30	1300	M	1	2	C	N	Y	N	0	N	N	N	N	0	1	N	N	Y	N	N	2	4	2	0	6	1	III	2	N	III	0	N	Y	N	24	O	N
815	32	1800	M	1	0	V	N	N	Y	0	Y	Y	N	N	0	1	N	Y	N	N	N	2	1	0	0	5	1	III	0	N	III	2	Y	N	N	31	O	N
816	29	1100	F	1	0	V	N	Y	N	0	N	Y	N	N	0	1	N	N	N	N	Y	0	0	1	0	2	0	II	0	N	II	0	N	N	N	35	O	N
817	36	1580	M	2	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	40	O	N
818	30	1470	M	2	2	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	1	0	0	0	0	III	0	N	II	0	N	N	N	0	O	N
819	30	1280	M	2	2	C	N	N	Y	0	N	Y	N	N	0	0	N	N	N	N	N	0	2	0	0	0	0	II	0	N	II	0	N	N	N	0	O	N
820	27	750	F	1	4	C	N	Y	Y	10	Y	N	N	N	0	0	N	N	N	Y	Y	4	1	0	0	0	0	I	0	N	II	0	N	Y	N	31	O	N
821	33	1400	F	1	2	C	N	Y	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	2	0	0	0	0	III	0	N	III	0	N	N	N	0	O	N
822	34	1500	M	1	3	C	N	N	N	11	N	N	N	Y	1	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	O	N
823	34	1700	M	1	0	C	N	N	N	12	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	O	N
824	32	1800	M	1	0	V	N	Y	N	0	N	Y	N	Y	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	III	2	N	Y	N	35	O	N
825	30	1300	M	1	2	C	N	N	N	0	Y	Y	N	Y	1	1	N	Y	N	N	Y	5	8	2	0	4	0	III	2	N	III	0	N	Y	N	35	O	N
901	38	3100	M	1	0	C	N	N	N	0	Y	Y	N	Y	1	2	N	N	Y	N	Y	7	5	1	0	1	0	II	0	N	M	0	N	N	N	0	O	N
902	32	1430	M	1	0	V	N	Y	N	0	Y	Y	N	N	0	2	N	N	N	N	Y	3	5	1	0	1	0	II	0	N	II	0	N	N	Y	40	O	N
903	30	1630	M	1	0	C	N	Y	N	0	Y	Y	N	N	0	1	N	N	N	N	N	3	3	1	0	2	0	II	0	N	II	0	N	N	N	0	O	N
904	33	1800	M	1	0	C	N	Y	N	0	Y	Y	N	N	0	0	N	N	N	N	N	0	5	0	0	0	0	II	0	N	II	0	N	N	N	0	O	N
905	32	880	F	1	1	C	N	Y	N	0	N	Y	N	N	0	0	N	N	N	N	Y	8	11	2	0	6	0	II	0	N	II	0	N	N	N	0	O	N
906	34	1900	M	1	0	V	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	O	N
907	35	1700	M	1	0	C	N	Y	N	0	N	Y	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	N	N	0	O	N
908	32	1330	M	1	4	C	N	Y	Y	0	Y	Y	N	N	0	1	N	N	N	N	Y	1	16	1	0	2	1	I	0	N	II	0	N	Y	N	37	O	N
909	32	1210	F	1	0	C	Y	Y	N	0	Y	N	N	N	0	1	N	N	N	N	N	5	2	0	0	0	0	II	0	N	II	0	N	N	N	0	O	N
910	29	1200	F	1	0	V	N	Y	N	0	N	N	N	N	1	1	N	N	N	N	N	0	10	1	0	2	0	II	0	N	II	0	N	Y	N	33	L	N
911	33	1400	F	2	0	C	N	N	Y	0	Y	N	N	N	0	0	N	N	N	N	N	0	2	0	0	0	0	III	0	N	III	0	N	N	N	0	O	N
912	33	1500	M	2	0	C	N	N	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	2	0	0	0	0	III	0	N	III	0	N	N	N	0	O	N
913	35	1500	F	1	0	C	N	N	N	11	N	N	N	N	0	0	N	N	N	N	N	0	1	0	0	0	0	M	0	N	M	0	N	N	N	0	O	N
914	30	1200	M	3	0	V	N	N	N	0	Y	Y	N	N	0	0	N	N	N	N	N	2	4	0	0	0	0	III	0	N	III	0	Y	N	N	34	O	N

No.	GA	BW	GENDER	PARITY	STEROIDS	MOD	GDM	MHTN	PPROM	OMF	RDS	AOP	ASPHYXIA	PDA	PDAT	SEPSIS	IVH	ANEMIA	NNS	SURFACT	B& M	PMA	O2	BLOOD	FFP	PLATELET	PACKED CELL	RE ZONE	RE STAGE	RE PLUS	LE ZONE	LE STAGE	LE PLUS	ANY ROP	TYPE I ROP	PCA D	PCA T	TREAT	RE TREAT
915	30	1100	M	3	0	V	N	N	N	0	Y	Y	N	N	0	0	N	N	N	N	N	0	4	0	0	0	0	II	0	N	II	0	N	Y	N	32	0	O	N
917	28	1130	F	2	0	C	Y	Y	N	0	Y	Y	N	N	1	0	N	N	N	N	Y	4	13	0	0	6	0	II	0	N	II	0	N	Y	Y	32	0	I	N
918	31	950	F	1	0	C	N	Y	N	0	Y	N	N	N	0	1	N	N	N	N	N	2	1	0	1	0	1	III	0	N	III	0	N	N	N	0	0	O	N
919	27	910	F	2	1	C	N	Y	N	0	Y	Y	N	N	1	1	N	Y	N	N	Y	12	32	2	0	5	2	II	0	N	I	1	N	Y	N	35	0	O	N
921	28	790	M	2	0	C	N	Y	N	0	Y	Y	N	N	1	3	N	N	N	N	Y	7	15	1	0	1	0	I	0	N	I	0	N	Y	Y	31	31	B	N
922	30	1025	F	1	2	V	N	N	N	0	Y	N	N	N	0	2	N	Y	N	N	N	0	25	2	1	2	2	II	0	N	II	0	N	Y	N	35	0	O	N
923	27	1000	F	1	2	V	N	N	N	0	N	Y	N	N	0	1	N	N	N	N	N	14	4	2	0	7	0	II	0	N	II	0	N	Y	N	33	0	O	N
924	33	1260	M	1	0	C	N	Y	N	0	N	N	N	N	0	0	N	N	N	N	N	0	18	0	0	0	0	III	0	N	III	1	N	Y	N	36	0	O	N
1001	33	2260	M	1	0	C	N	N	N	0	Y	N	N	N	0	1	N	N	N	N	N	0	7	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
1002	28	910	M	1	2	V	N	Y	N	0	Y	N	N	N	1	0	N	Y	N	N	N	8	1	1	0	3	0	II	0	Y	II	0	N	Y	N	33	0	O	N
1003	33	2000	M	1	0	C	N	N	N	2	Y	N	N	N	0	0	N	N	N	N	N	0	7	0	0	0	0	II	0	N	III	0	N	N	N	0	0	O	N
1004	36	1600	M	1	2	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
1005	28	1230	M	2	0	C	N	N	N	0	N	N	N	N	0	1	N	Y	N	N	N	0	0	1	0	1	1	II	0	N	II	0	N	Y	N	36	0	O	N
1006	28	1320	M	2	0	C	N	N	N	0	Y	N	N	N	0	1	N	N	N	N	N	1	0	2	2	6	2	II	0	N	II	0	N	Y	N	35	0	O	N
1007	30	1670	M	1	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
1009	34	1600	M	2	0	V	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
1010	34	2100	M	2	0	V	N	N	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
1011	31	1520	F	1	0	C	N	N	N	0	Y	Y	N	N	1	0	N	Y	N	N	N	1	4	1	0	2	4	III	0	N	III	0	N	N	N	0	0	O	N
1012	32	1100	M	1	0	V	N	Y	N	0	Y	N	N	N	0	2	N	Y	N	N	Y	3	4	2	0	5	1	II	0	N	II	0	N	N	N	0	0	O	N
1013	35	1700	M	1	0	C	N	N	N	0	Y	N	N	N	0	0	N	N	N	N	Y	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
1014	30	1670	M	1	2	C	N	N	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	8	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
1015	32	1200	M	1	0	C	N	N	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
1016	30	1700	M	1	0	V	N	N	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
1017	28	1030	F	1	0	V	N	Y	N	0	N	Y	N	N	0	1	N	N	N	N	N	0	18	2	0	7	0	II	0	N	II	0	N	Y	N	34	0	O	N
1018	33	1300	M	1	0	C	Y	Y	N	2	N	N	N	N	0	0	N	N	N	N	N	0	1	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
1019	34	2190	M	1	0	C	N	N	N	0	N	Y	N	N	0	0	N	N	N	N	Y	2	1	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
1020	34	1880	F	2	0	C	Y	N	Y	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
1021	34	2000	F	2	0	C	Y	N	Y	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
1022	33	1500	F	1	2	C	N	Y	N	6	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	III	0	N	III	0	N	Y	N	38	0	O	N
1023	29	1100	M	1	0	V	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
1024	40	2500	F	1	0	V	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
1025	30	1200	F	1	2	V	N	Y	N	0	N	N	N	N	0	0	N	N	N	N	N	0	2	2	1	4	0	II	0	N	II	0	N	Y	Y	36	38	L	N

No.	GA	BW	GENDER	PARITY	STEROIDS	MOD	GDM	MHTN	PPROM	OMF	RDS	AOP	ASPHYXIA	PDA	PDAT	SEPSIS	IVH	ANEMIA	NNS	SUREFACT	Bk M	PMA	O2	BLOOD	FFP	PLATELET	PACKED CELL	RE ZONE	RE STAGE	RE PLUS	LE ZONE	LE STAGE	LE PLUS	ANY ROP	TYPE I ROP	PCA D	PCA T	TREAT	RE TREAT
1101	31	1480	M	1	3	V	N	N	Y	3	Y	N	N	Y	1	1	N	N	N	N	N	7	4	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
1102	30	1240	F	1	2	C	N	N	N	0	Y	N	Y	Y	0	1	N	N	N	N	N	0	5	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
1103	34	1480	M	1	0	V	N	N	N	0	N	Y	N	N	0	0	N	N	N	N	N	7	2	1	0	5	II	0	N	III	0	N	N	N	0	0	O	N
1104	32	1260	F	1	2	C	N	Y	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
1105	33	1640	F	1	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
1106	35	2340	M	1	0	C	N	N	Y	0	Y	N	N	N	0	1	N	N	N	N	N	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
1107	40	2700	M	1	0	V	N	N	N	3	Y	N	N	N	0	2	N	N	N	N	Y	15	16	1	0	3	M	0	N	M	0	N	N	N	0	0	O	N
1108	34	1660	F	2	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
1109	36	1350	M	0	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	III	0	N	II	0	N	N	N	0	0	O	N
1110	34	2960	M	1	1	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	8	4	0	0	0	III	0	N	II	0	N	N	N	0	0	O	N
1111	33	997	M	1	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
1112	29	1100	M	1	0	V	N	N	N	0	N	Y	N	N	0	0	N	N	N	N	N	0	7	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
1113	33	1780	F	1	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
1114	36	1800	M	1	0	V	N	N	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	3	0	0	0	III	0	N	II	0	N	N	N	0	0	O	N
1115	34	1800	F	1	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
1116	34	2400	M	1	0	C	N	N	Y	0	Y	N	Y	N	0	0	N	N	N	N	N	0	6	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
1117	38	2500	M	1	0	C	N	N	N	0	Y	N	N	Y	0	0	N	N	N	N	N	1	5	0	0	0	M	0	N	M	0	N	N	N	0	0	O	N
1118	32	2020	M	1	0	C	N	N	Y	0	Y	N	Y	Y	0	0	N	N	N	N	N	0	3	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
1119	34	1430	F	1	0	C	Y	N	Y	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	M	0	N	M	0	N	N	Y	0	0	O	N
1120	30	1200	F	2	3	V	Y	N	N	0	N	N	N	N	0	1	N	N	N	N	N	0	0	0	0	0	II	0	N	II	0	N	N	Y	38	0	O	N
1121	30	1100	M	2	3	V	Y	N	N	0	Y	N	N	Y	1	1	N	N	N	N	Y	3	5	0	0	0	II	0	N	II	0	N	N	Y	35	36	L	N
1122	24	1600	M	1	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	III	0	N	III	0	N	N	N	0	0	O	N
1124	28	950	M	1	2	V	N	N	N	0	N	N	Y	Y	1	1	N	N	N	N	N	2	5	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
1125	31	1040	M	1	2	V	N	N	N	0	Y	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	II	0	N	II	0	N	N	N	0	0	O	N
1126	35	1300	M	1	0	C	N	N	N	0	N	N	N	N	0	0	N	N	N	N	N	0	0	0	0	0	III	0	N	II	0	N	N	N	0	0	O	N
1127	30	1240	F	1	2	V	N	Y	N	0	Y	N	N	Y	0	1	N	N	N	N	N	0	10	0	0	0	III	2	N	III	2	N	N	Y	0	37	O	N