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Study of Incidence, Risk Factors, With Special Reference To Role Of Anemia In The Development Of Retinopathy Of Prematurity

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ABSTRACT

Background: ROP, or Retinopathy of Prematurity, is a major cause of avoidable childhood blindness, especially in infants born prematurely or with low birth weights. For prompt diagnosis and treatment, early risk factor identification is crucial.

Methods: To ascertain the incidence and risk variables linked to ROP, a prospective hospital-based study was carried out at SCB Medical College and SVPPGIP, Cuttack, between September 2015 and September 2017. A total of 374 newborns who met the screening requirements were assessed. A total of 124 newborns were included in the final analysis after completing follow-up exams. Risk factors for mothers, newborns, and clinicians were evaluated.

Results: ROP was present in 27.4% of cases overall. ROP development was substantially correlated with lower birth weight and gestational age. Infants with birth weights under 1000 g and gestational ages under 28 weeks had a greater incidence. Prolonged oxygen therapy, apnea, respiratory distress syndrome, and blood transfusion were significant newborn risk factors. Term infants with known risk factors also showed signs of ROP. ROP newborns had decreased mean hemoglobin levels, however anemia by itself was not determined to be a risk factor. While some patients showed spontaneous regression, the majority of cases were Stage I or II ROP, and severe cases needed surgery or laser therapy.

Conclusion: ROP is still a serious health risk for low birth weight and preterm babies. It can also happen to term babies who have risk factors. Significant factors include blood transfusions, oxygen therapy, birth weight, gestational age, and respiratory issues. Early screening, increased provider awareness, and organized follow-up programs are necessary to guarantee prompt treatment and lessen the incidence of avoidable pediatric blindness.

KEYWORDS: Pediatric Blindness, Retinopathy of Prematurity, Infant, Respiratory Issues, Gestational Age.

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INTRODUCTION

Previously known as retrolental fibroplasia, retinopathy of prematurity (ROP) is a multifactorial vasoproliferative retinal condition that becomes more common as gestational age (GA) decreases. Vasoconstriction, elevated levels of vasogenic factors such as vascular endothelial growth factor, and compensatory neovascularization are proposed as potential mechanisms of injury, which can result in retinal detachment and severe extraretinal fibrovascular proliferation (1). With a frequency ranging from 35 to 60%, ROP is primarily restricted to preterm infants with birth weight (BW) of less than 1500 grams or gestational age (GA) of fewer than 32 weeks. In India, ROP is becoming one of the main causes of avoidable childhood blindness (2).

While breastfeeding and a history of maternal preeclampsia are protective factors, a number of risk factors are linked to ROP, including low GA, low birth weight, prolonged oxygen exposure, severe respiratory distress requiring mechanical ventilation, shock, sepsis, hypoxia, prolonged ventilatory support, need for blood transfusion, intraventricular hemorrhage, acidosis, anemia, high ambient light, and vitamin E deficiency (3).

The median age for stage 1 ROP discovery is 34 weeks, pre-threshold ROP is 36 weeks, and threshold disease is 37 weeks. Almost no cases of ROP are found prior to 32 weeks of GA. By the 40th week of GA, retinal vascularization is complete. Therefore, the critical window for ROP detection is between 32 and 40 weeks. The key period, during which the condition progresses and treatment may need to be initiated, is between 34 and 38 weeks of age (4).

The risk factors that require therapy include the presence of ROP on the initial examination, posterior location, increasing stage severity, circumferential involvement, plus disease, and rapid development. High myopia, refractive errors, strabismus, amblyopia, astigmatism, retinal detachment, and glaucoma are all more likely to occur in infants with substantial ROP. In high-

developed nations, ROP accounts for 3% to 11% of juvenile blindness, but in middle-developed nations, it can reach 60%. As of this now, there are no proven ways to prevent ROP (5). It has been demonstrated that careful monitoring of risk factors, early screening, follow-up, and surgical intervention can lower the incidence and improve the outcome of ROP because the majority of the risk factors for ROP listed above occur in the neonatal intensive care unit (NICU) itself and are mostly preventable (6). The current study is being conducted in the NMW, SNCU, and NICU of SCB Medical College, Cuttack & SVPPGIP, Cuttack, because to the dearth of Indian studies on the incidence and risk factors of ROP from Government tertiary care institutes.

MATERIALS AND METHOD

The research methods are adopted as per the objectives of the study.

Place of Study:
The Newborn Ward, SNCU & NICU of SCB Medical College &
Sardar Vallabh Bhai Patel Postgraduate Institute of Paediatrics (SVPPGIP), Cuttack.

Period of Study:
Two years (from September 2015 to September 2017)

Study Design:
A hospital based prospective study.

Inclusion Criteria:
1. The study included all preterm neonates delivered or admitted to SCB Medical College in Cuttack with a gestational age of fewer than 37 completed weeks, regardless of birth weight.
2. Included are all term newborns, defined as those with a gestational age of 37 weeks or more and risk factors such anemia, sepsis, or oxygen dependency.
3. The patients whose parents agree to let their children participate in this research.

Exclusion Criteria: -
1. All patients who are 37 weeks or older and do not have any of the risk factors listed above.
2. Patients who have serious congenital defects or are in critical condition.
3. whose parents refuse to consent to the study.
4. Infants lost to follow-up prior to 42 weeks of postmenstrual age or complete retinal vascularization.
5. Infants who passed away for whatever reason during follow-up or following the initial ophthalmological test.

Statistical Analysis:
SPSS 20.0.1 and a Microsoft Excel spreadsheet were used for statistical analysis. Fisher's exact test and a chi-square calculator were used for univariate analysis. After the trial was over, the data was examined for potential risk factors, paying particular attention to the part anemia played. A statistically significant p value was defined as less than 0.05.

RESULTS

Table 1: Demographic distribution

TOTAL PATIENTS	124	**100%**
ROP PRESENT	34	**27.4%**
ROP ABSENT	90	**72.6%**

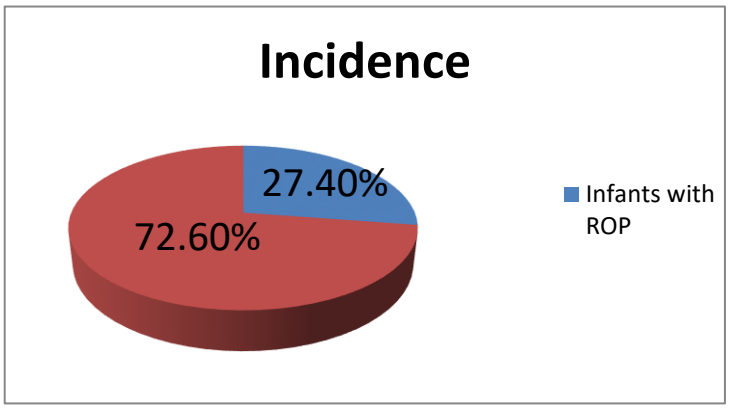


Figure 1: Incidence of ROP in infants

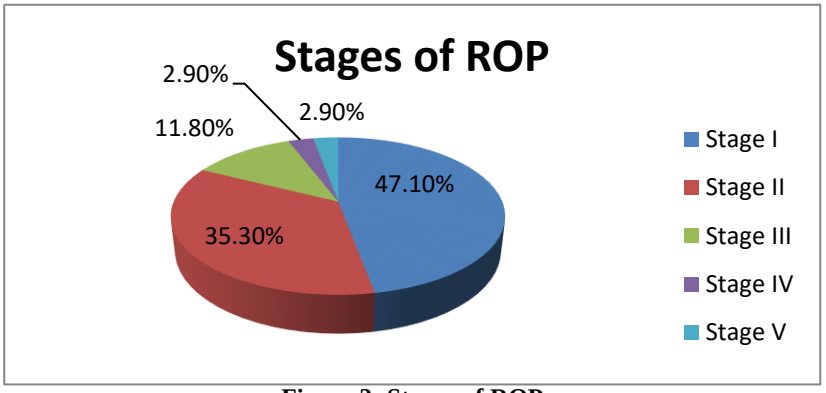


Figure 2: Stages of ROP

Table 2: Distribution of ROP stages

STAGES	NO OF INFANTS	% OF ROP
STAGE I	16	47.1%
STAGE II	12	35.3%
STAGE III	4	11.8%
STAGE IV	1	2.9%
STAGE V	1	2.9%
TOTAL	34	100%

Sex Distribution:

Out of124 babies analysed, 72 babies were male & 52 were female. The male:female ratio is 1.38:1.0 . Out of 72 males, 20 babies developed ROP(27.8%) & out of 52 females, 14 developed ROP(26.9%).

Table 3: Distribution of ROP

SEX	NO OF INFANTS OBSERVED	NO OF INFANTS WITH ROP	ROP(in %)
MALE	72	20	27.8%
FEMALE	52	14	26.9%
TOTAL	**124**	**34**	**27.4%**

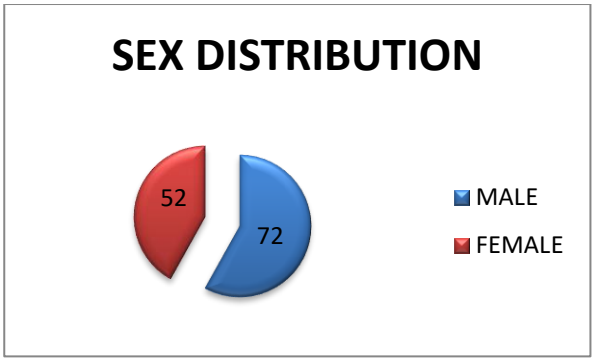


Figure 3: Sex distribution of ROP

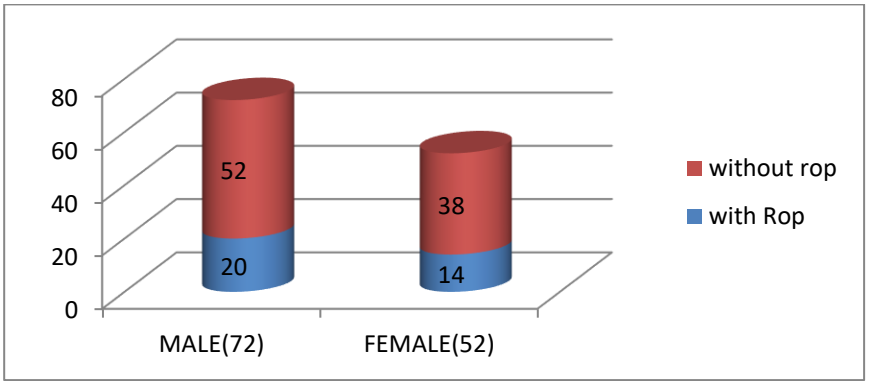


Figure 4: Sex distribution with or without ROP

Birth Weight

The incidence of ROP in the babies decreases as the birth weight of the neonate increases.ROP developed in infants who were <1000g was **58.3%**, between 1001g-1500g was **20.4%**, >1500g was **17.6%**.

Table 4: Distribution of weight in ROP patients

X^2 =14.348

p value= 0.000766(extremely statistically significant)

INCIDENCE OF ROP ACC. TO BIRTH WEIGHT

BIRTH WEIGHT (in gms)	ROP PRESENT	ROP ABSENT	TOTAL(%)
<1000g	14(58.3%)	10(41.7%)	24(19.4%)
1001-1500g	17(20.4%)	66(79.6%)	83(66.9%)
>1500g	3(17.6%)	14(82.4%)	17(13.7%)
TOTAL	**34**	**90**	**124(100%)**

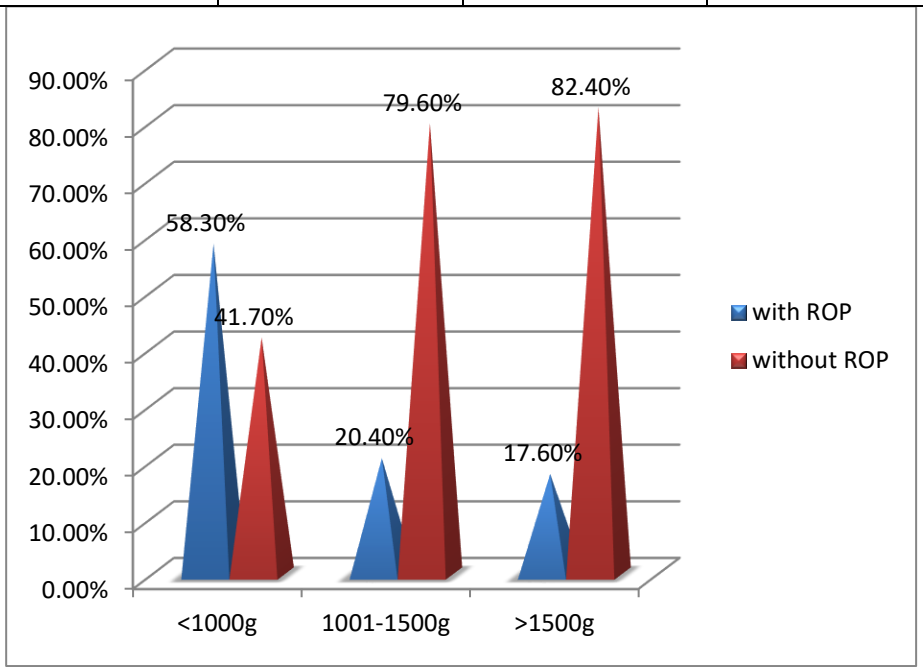


Figure 5: Distribution of weight in ROP patients

Gestational Age:

The incidence of ROP in infants <28 wks was **59.4%**, infants between 28-32 wks was **15.8%**, infants between 32-37 wks was **15.4%**. However there was an increase in incidence among term infants with risk factors i.e **33.3%**.

Table 5: Incidence of ROP

GESTATIONAL AGE	ROP PRESENT	ROP ABSENT	TOTAL
< 28 weeks	19(59.4%)	13(40.6%)	32(25.8%)
28-32 weeks	12(15.8%)	64(84.2%)	76(61.3%)
32-37 weeks	2(15.4%)	11(84.6%)	13(10.5%)
>37 weeks	1(33.3%)	2(66.7%)	3(2.4%)
TOTAL	**34**	**90**	**124(100%)**

X^2= 22.5838

P value= 0.000049 (extremely statisticaly significant)

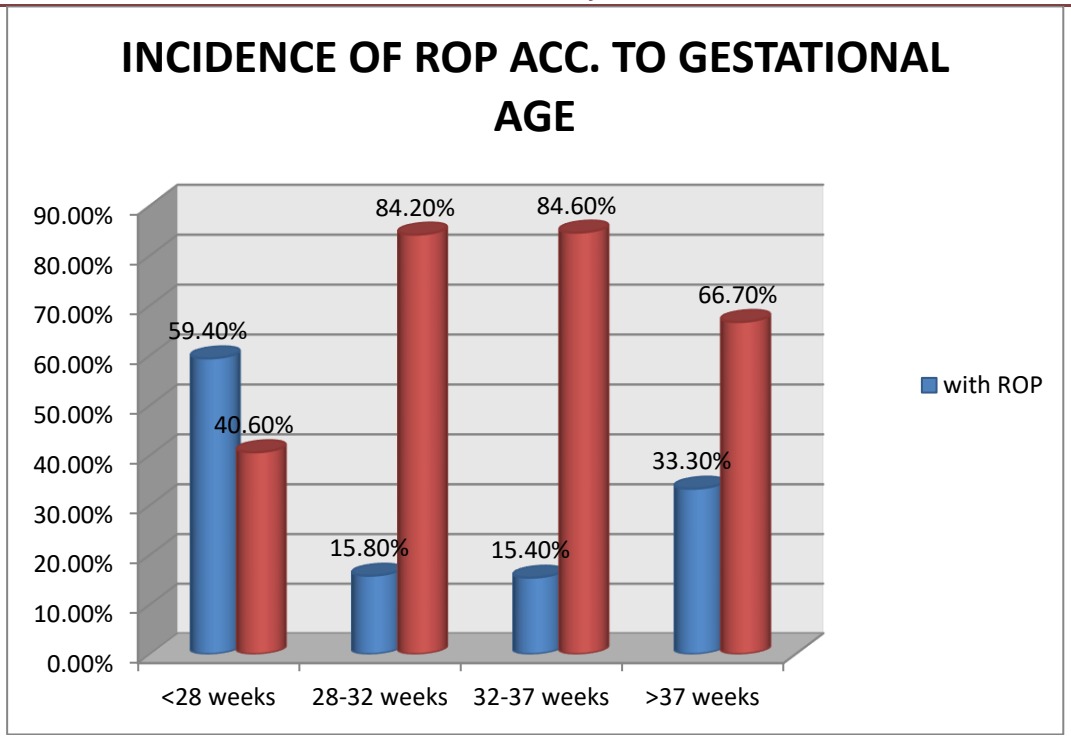


Figure 6: Incidence of ROP according to gestational age

Haemoglobin/ Hematocrit

The incidence of ROP in anemic babies was significantly higher i.e **13.9%**, & ROP in non anemic babies was **32.9%**.

Table 6: Incidence of hemoglobin in ROP

Hb / Hct	ROP PRESENT	ROP ABSENT	TOTAL
<10/ <30	6(16.7%)	30(83.3%)	36(29%)
≥10/ ≥30	28(31.8%)	60(68.2%)	88(71%)
TOTAL	**34**	**90**	**124(100%)**

X^2=2.9471

p value= 0.0860(not significant)

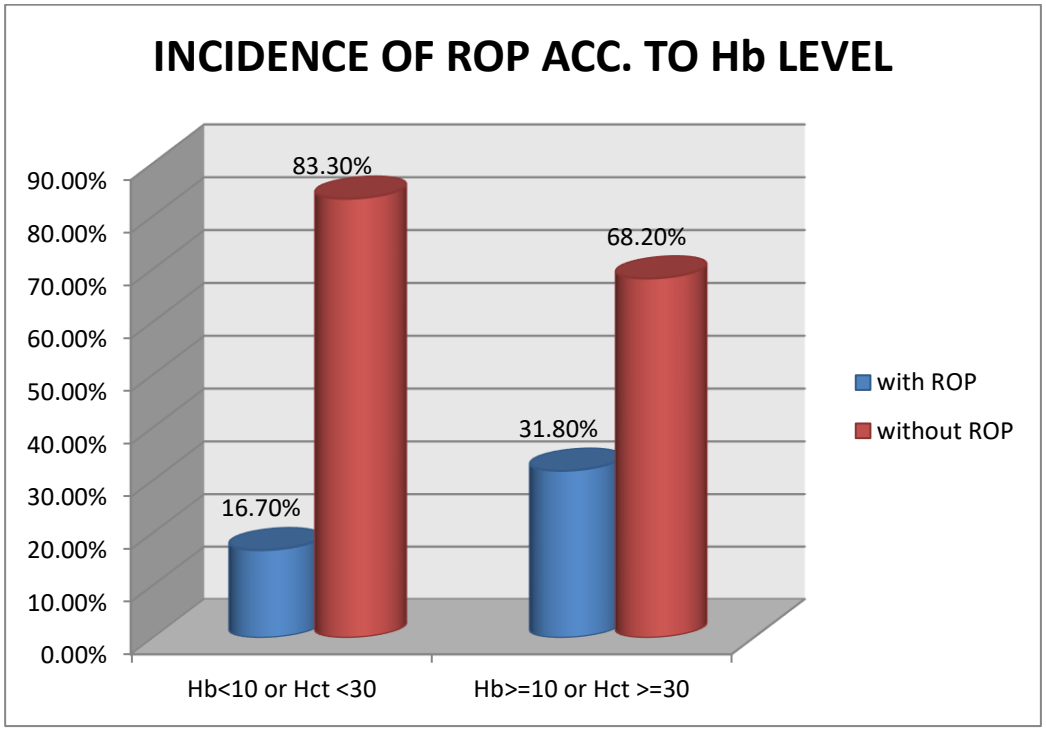


Figure 7: Incidence of ROP according to Hb level

Blood Transfusion

Out of 124 babies, 30 babies received blood transfusion. Out of these 30 babies, 15 babies i.e **50.0%** developed ROP, whereas only **20.2%** of non transfused babies developed ROP.

Table 7: Incidence of ROP according to blood transfusion

H/O of BT	ROP PRESENT	ROP ABSENT	TOTAL
YES	15(50.0%)	15	30(24.2%)
NO	19(20.2%)	75	94(75.8%)
TOTAL	**34**	**90**	**124(100%)**

X^2=10.13 ; p value=0.0014(statistically significant)

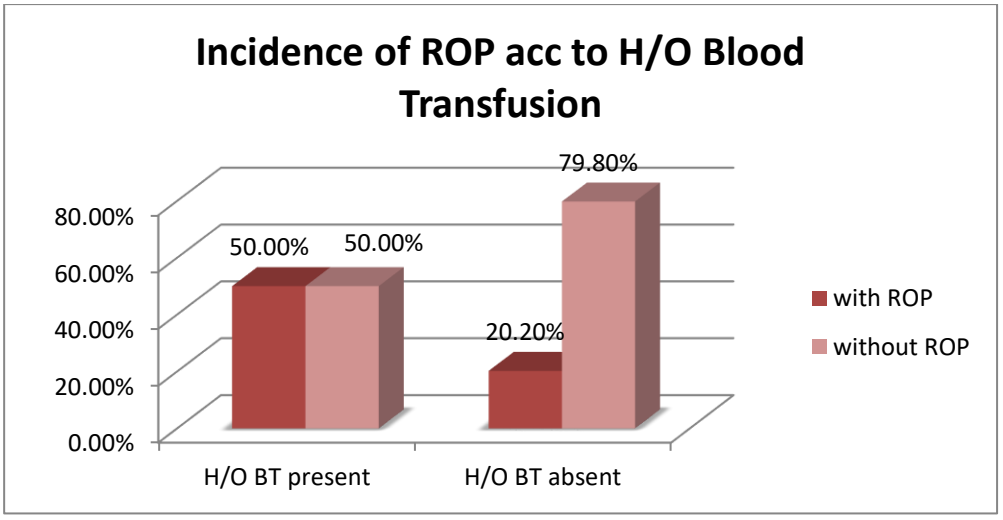


Figure 8: Incidence of ROP according to Hb blood transfusion

SEPSIS: 22 out of 64 babies with sepsis developed ROP(**34.4%),** whereas only 12 out of 60 babies without sepsis developed ROP(**20.0%).**

Table 8: Incidence of sepsis screening

SEPSIS SCREEN POSITIVE*	ROP PRESENT	ROP ABSENT	TOTAL
YES	22(34.4%)	42	64(51.6%)
NO	12(20.0%)	48	60(48.4%)
TOTAL	**34**	**90**	**124(100%)**

***culture proven/ clinical suspicion& screen positive/culture negative sepsis treated with antibiotics for>5-7 days.

X^2=3.215 ; p value=0.0729(not significant)

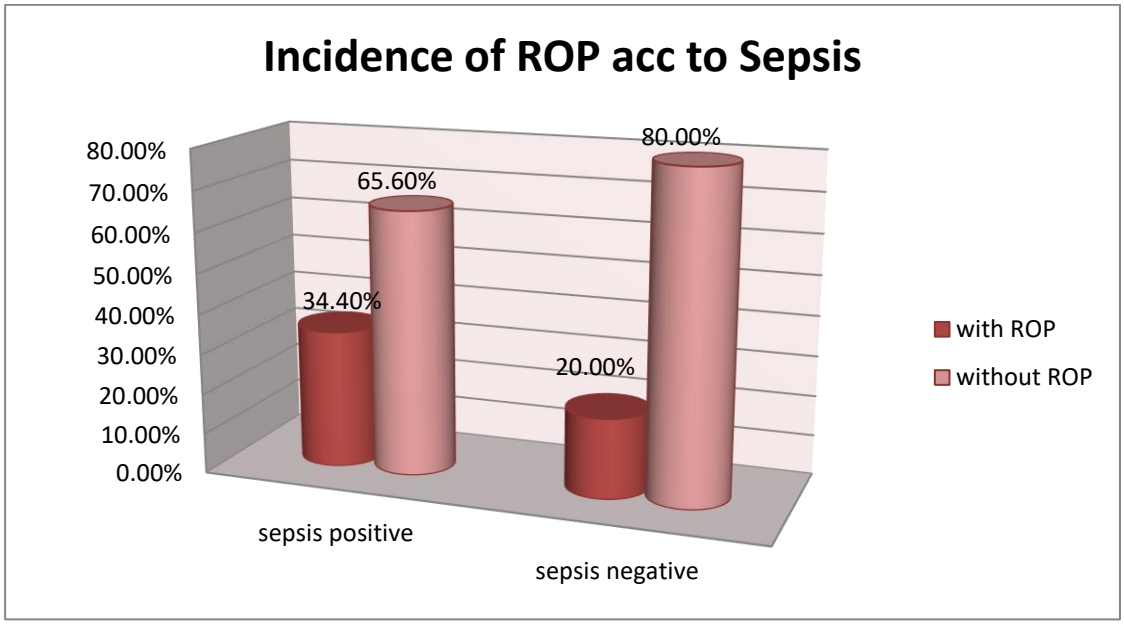


Figure 9: Incidence of ROP according to sepsis

APNEA: 22 out of 42 babies who had apnea developed ROP (**52.4%),** whereas only 12 out of 82 babies without apnea developed ROP (**14.6%).**

Table 9: Incidence of apnea

APNEA	ROP PRESENT	ROP ABSENT	TOTAL
YES	22(52.4%)	20	42(33.9%)
NO	12(14.6%)	70	82(66.1%)
TOTAL	**34**	**90**	**124(100%)**

X^2 =19.88 ; p value< 0.00001(extremely statistically significant)

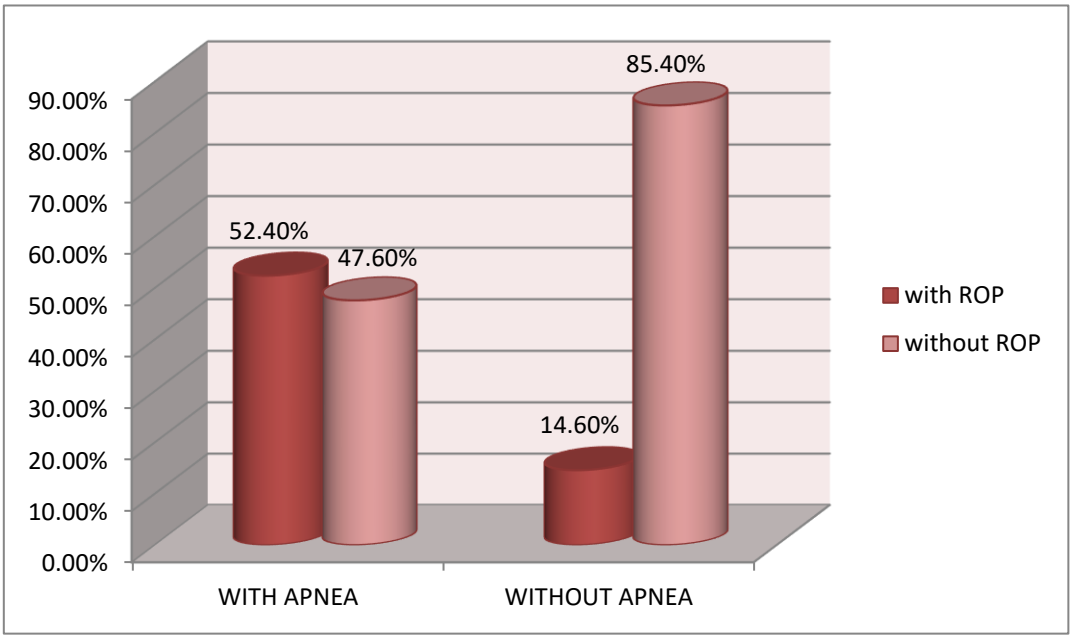


Figure 10: Incidence of ROP according to apnea

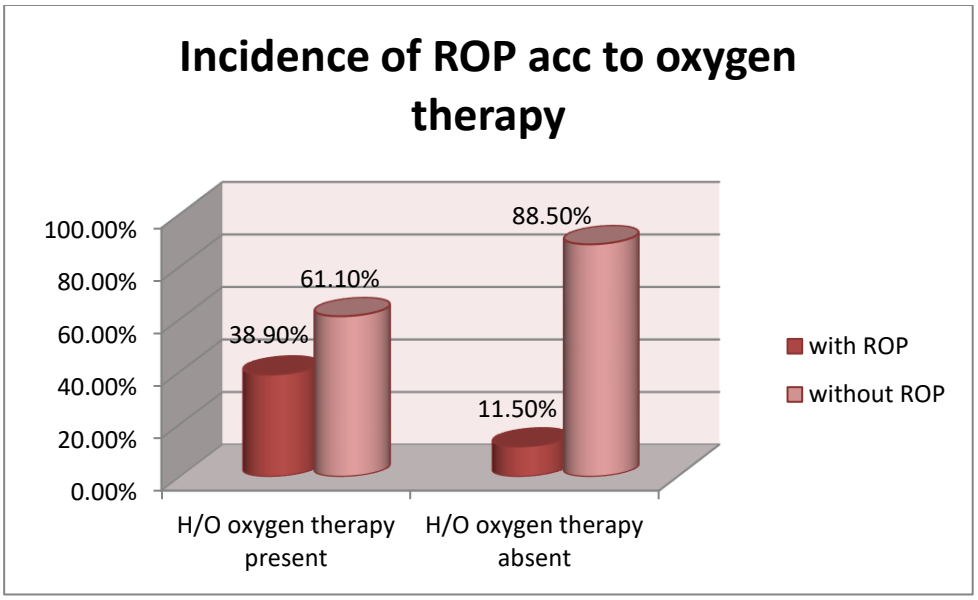
Supplemental Oxygen Therapy: 28 out of 72 babies who received oxygen therapy developed ROP(**38.9%),** whereas 6 out of 52 babies without oxygen therapy developed ROP(**11.5%**).

Table 10: O_2 therapy in ROP patients

O_2 THERAPY*	ROP PRESENT	ROP ABSENT	TOTAL
YES	28(38.9%)	44	72(58.1%)
NO	6(11.5%)	46	52(41.9%)
TOTAL	**34**	**90**	**124(100%)**

***supplemental oxygen therapy for more than equal to 5 days.

X^2= 11.34; p value= 0.000755(extremely statistically significant)

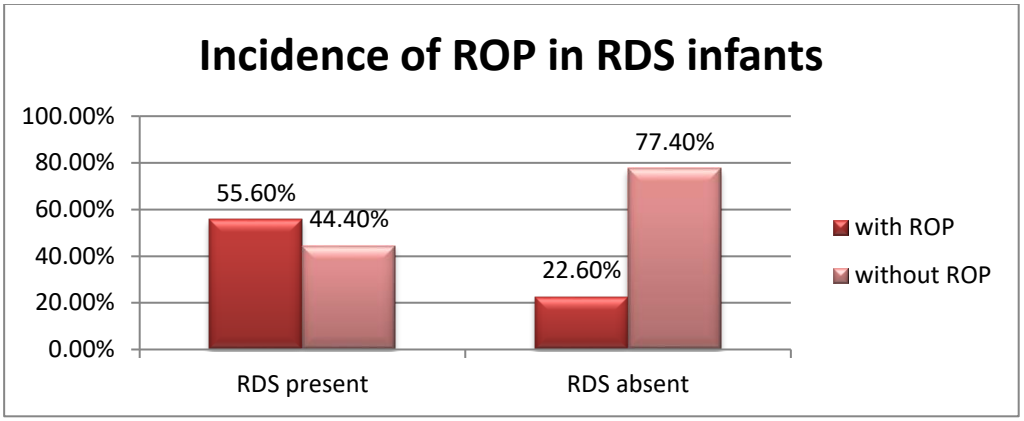


Respiratory Distress Syndrome

10 out of 18 babies with RDS developed ROP(55.6%) & 24 out of 106 babies developed ROP(22.6%).

RDS	ROP PRESENT	ROP ABSENT	TOTAL
YES	10(55.6%)	8	18(14.5%)
NO	24(22.6%)	82	106(85.5%)
TOTAL	**34**	**90**	**124(100%)**

X^2= 8.3761; p value= 0.003(statistically significant)

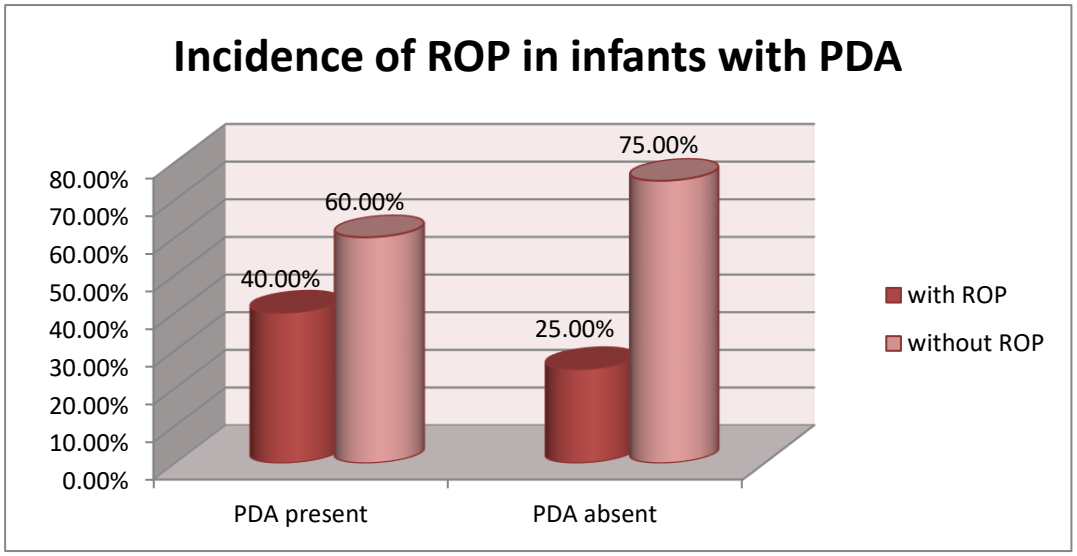


PERSISTENT DUCTUS ARTERIOSUS:

8 out of 20 babies with PDA developed ROP (40.0%) whereas 26 out of 104 babies developed ROP(25.0%).

PDA	ROP PRESENT	ROP ABSENT	TOTAL
YES	8(40.0%)	12	20(16.1%)
NO	26(25.0%)	78	104(83.9%)
TOTAL	**34**	**90**	**124(100%)**

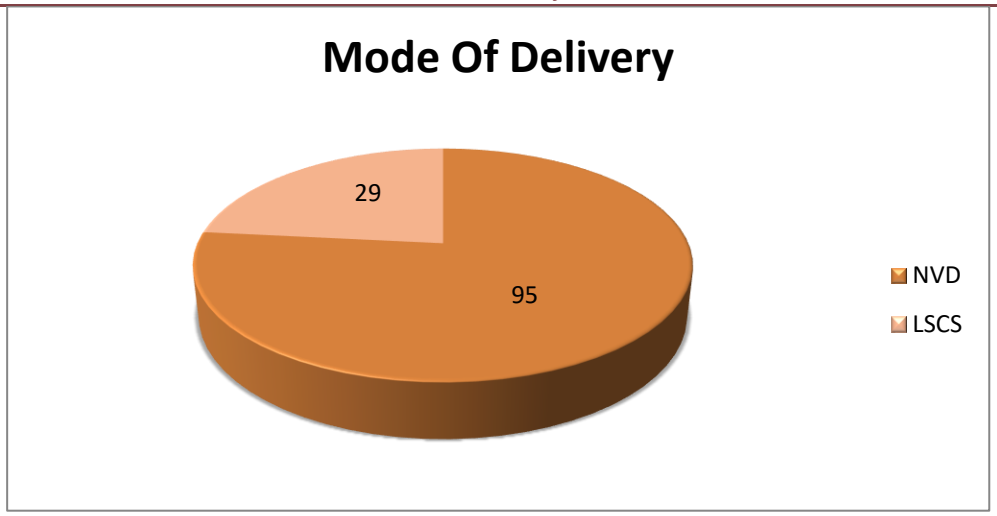
***X^2*=1.8965; p value= 0.168(not significant)**



Mode of Delivery

Out of 124 babies screened, 95 babies were born by NVD & 29 babies were born by LSCS. 26.3% of NVD-born babies developed ROP & 31% of LSCS-born developed ROP.

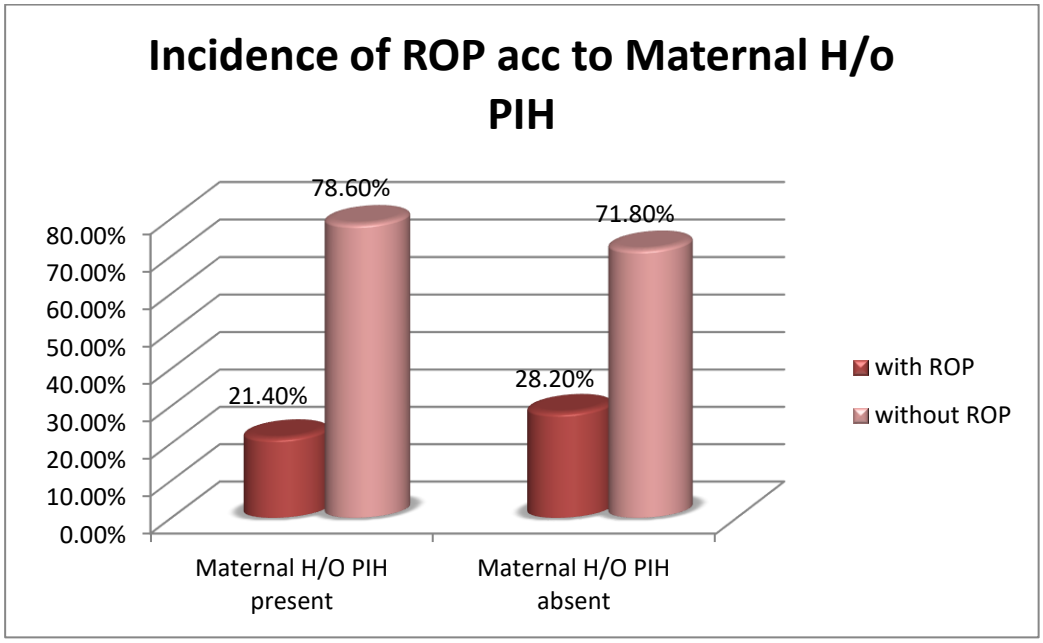
MODE OF DELIVERY	NO OF INFANTS OBSERVED	NO OF INFANTS WITH ROP	TOTAL
NVD	95	25	**26.3%**
LSCS	29	9	**31.0%**
TOTAL	124	34	**27.4%**



PIH (PREGNANCY INDUCED HYPERTENSION): 21.4% of babies with maternal PIH developed ROP & **28.2%** of babies without maternal PIH developed ROP.

H/O of PIH	ROP PRESENT	ROP ABSENT	TOTAL
YES	3(21.4%)	11	14(11.3%)
NO	31(28.2%)	79	110(88.7%)
TOTAL	**34**	**90**	**124(100%)**

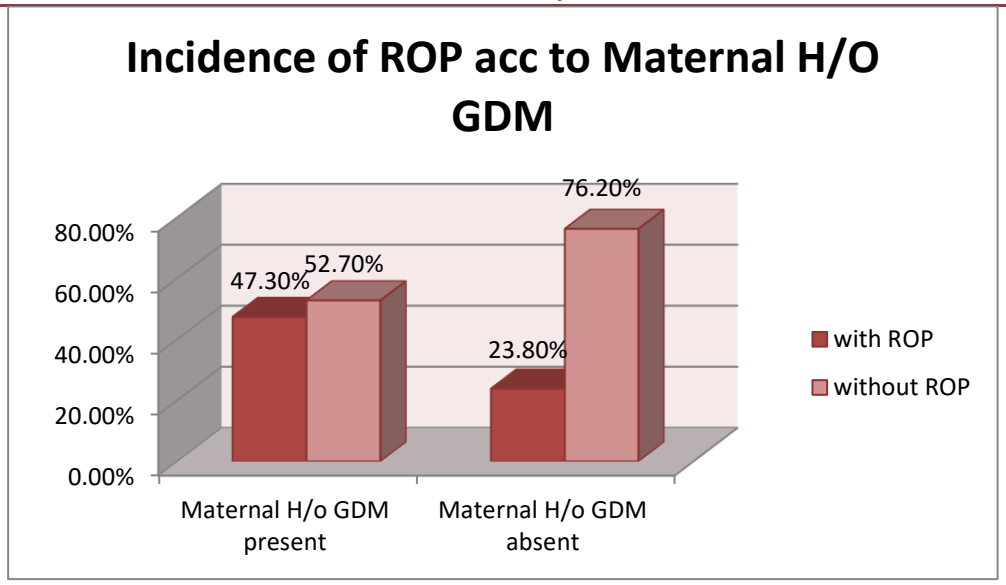
X^2=0.284 ; p value= 0.5936(not significant)



GESTATIONAL DIABETES MELLITUS: 47.3% of babies with maternal GDM developed ROP whereas only 23.8% of babies without maternal GDM developed ROP.

H/O of GDM	ROP PRESENT	ROP ABSENT	TOTAL
YES	9(47.3%)	10	19(15.3%)
NO	25(23.8%)	80	105(84.7%)
TOTAL	**34**	**90**	**124(100%)**

X^2 =4.487 ; p value= 0.03415(statistically significant)

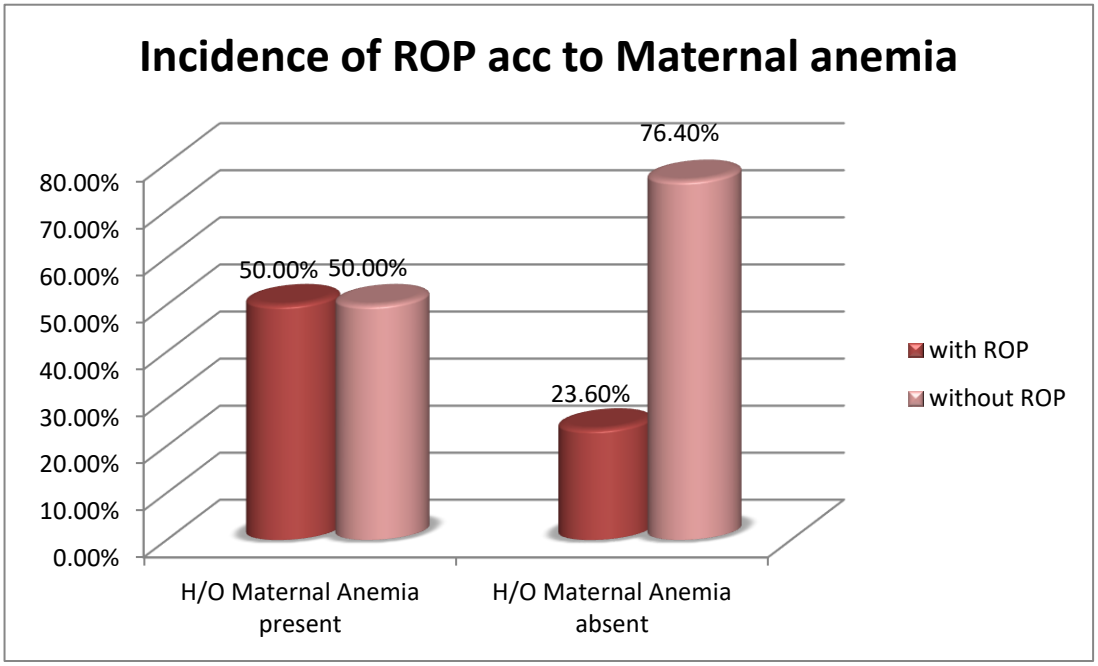


MATERNAL ANEMIA: 50.0% of babies with maternal anemia developed ROP & **23.6%** of babies without maternal anemia developed ROP.

H/O of MATERNAL ANEMIA*	ROP PRESENT	ROP ABSENT	TOTAL
YES	9(50.0%)	9	18(14.5%)
NO	25(23.6%)	81	106(85.5%)
TOTAL	**34**	**90**	**124(100%)**

***Hb less than 10 g%.

X^2=5.394 ; p value=0.0201(statistically significant)



DISCUSSION

This hospital-based prospective study evaluated the incidence and risk factors of Retinopathy of Prematurity (ROP) among babies hospitalized to the NMW/SNCU/NICU at SCB Medical College and SVPPGIP, Cuttack between September 2015 and September 2017. 250 (66.8%) of the 374 kids that were screened either died before the test was completed or were lost to follow-up. This dropout rate is comparable to other research group, who reported a 78.6% dropout rate, which they mostly attributed to inadequate parental knowledge, significant diseases in babies, and financial difficulties (7),(8).

The overall incidence of ROP among the remaining 124 neonates included in the study was 27.4%, compared to other Indian studies. However, the incidence may have been lower than previous international and Indian publications due to the high infant

mortality, high dropout rate, and socioeconomic factors influencing early detection and follow-up (9).

There was no obvious gender preference, which is consistent with the findings of the CRYO-ROP experiment. Birth weight and gestational age showed a strong correlation with ROP. The highest incidence was seen in infants born before 28 weeks (59.4%) and those weighing less than 1000 grams at delivery (58.3%), both of which showed statistically significant relationships. These findings highlight the importance of close observation for premature and extremely low birth weight babies (10), (11).

Neonatal risk factors, including respiratory distress syndrome (RDS), apnea, packed cell transfusion, and prolonged oxygen therapy, were substantially associated with the development of ROP. However, no significant association was observed between the way of delivery, anemia, sepsis, or patent ductus arteriosus (PDA). Maternal factors such maternal anemia and gestational diabetes mellitus showed a significant connection with ROP, although pregnancy-induced hypertension did not (12).

In terms of the severity of the condition, Stage I ROP was the most common, followed by Stages II and III. In numerous instances, particularly in the first stages, spontaneous relapse occurred. One infant with Stage V ROP had irreparable visual loss, five required laser photocoagulation, and two required vitreoretinal surgery. The study emphasizes the need for early screening, increased parental awareness, and structured follow-up programs to prevent avoidable pediatric blindness. Additionally, it demonstrates the complex genesis of ROP (13).

CONCLUSION

This population-based study highlights the significant risk of retinopathy of prematurity (ROP) among neonates with extremely low birth weights, as there are strong associations between low birth weight and reduced gestational age. The study also revealed a noteworthy incidence of ROP in term infants with established risk factors, underscoring the significance of monitoring these babies as well. Factors include blood transfusions, respiratory distress syndrome, apnea, and prolonged oxygen therapy were significantly linked to the development of ROP. Anemia by itself was not a risk factor, despite the fact that ROP babies had lower mean hemoglobin levels. Increasing awareness and implementing effective screening programs are essential to ensuring early detection, timely treatment, and prevention of preventable pediatric blindness.

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