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A Study on Assessment and Progression of Retinopathy of Prematurity at Tertiary Care Centre

Authors
Dr Nikhil Dilip Charhate, Dr Ajit Gulabrao Khune, Dr Dhiraj Namdeo Balwir
Dr. Vasantrao Pawar Medical College, Nashik

Abstract
Background: *The study was conducted to assess the retinopathy of prematurity in pre mature infants and see the progression of the disease.*
Aims and Objectives: *To study the progression and the risk factors for Retinopathy of Prematurity (ROP) in infants.*
Material and Methods: *Prospective Observational Study from October 2020 to December 2022 done on 96 infants which was conducted in a tertiary care centre in NICU set up with the criteria: birth weight <1700g, gestational age at birth of <34-35 weeks, oxygen exposure of >30 days and infants with birth weight >1700g and gestational age >37 weeks with associated risk factors were assessed.*
Result: *Of 96 patients 24(25% incidence) found to be ROP positive with 13 requiring treatment had severe ROP. Average birth weight of ROP babies was 1491.45g and average gestational age was 31.41±2.82 weeks. 8/24 newborns had avascular retina later progressed to ROP.*
Conclusion: *Early assessment and detection of ROP is necessary to prevent further progression of disease.*
Keywords: *Retinopathy of prematurity, assessment, Progression, Risk factors.*

Introduction

Retrolental fibroplasia (RLF), today referred as retinopathy of prematurity (ROP), was the name given to it in the 1940s[(1)].The disease ROP is dynamic and time-bound; it does not exist at birth. ROP, a potentially blinding condition of the eyes, can affect newborns who were delivered 4 weeks or early to term and who received intensive neonatal care. To keep neonatal intensive care from growing, ROP assessment and treatment services must be scaled up.[(2)]

ROP incidence can be reduced by putting into practise quality improvement initiatives that limit exposure to recognised risk factors.[(3)] The survival rate of preterm babies has increased due to increased efforts by health ministries over the past 20 years to reduce newborn mortality in support of the Sustainable Development Goals and Millennium Development Goals, but at the same time, the number of infants at risk of ROP blindness has increased.[(4)]

The ROP incidence has been observed to range from 38% to 47% in India.[(5)]

If serious sequelae occur they have potential to lead to permanent blindness and all the related psychosocial, educational, and economic consequences if they are not treated or detected in time.[6]

Understanding the disease's course and the connection between risk factors and ROP would assist prevent the disease's progression and lower the incidence of ROP in INDIA.

Material and Methods

Study Design and Study Population

Study Type – Prospective Observational Study

Study Setting – Department of Ophthalmology of Medical College and Tertiary Health Care Centre

Study Duration – October 2020 to December 2022.

Study Population - From October 2020 to December 2022, assessments were conducted on all newborns meeting the inclusion criteria who are admitted to our NICU as well as those referred by outside OPDs.

Materials Used:-

1. Universal Infant wire speculum
2. Scleral indenter
3. Topical Anaesthesia (Paracaine)
4. 20D Condensing Lens for Screening
5. Indirect ophthalmoscope

Eligibility Criteria:

Between the months of October 2020 and December 2022, all neonates admitted to our Tertiary Care Center's NICU who weigh <1700 g and/or are ≤35 weeks gestation, as well as those referred from outside who visit our OPD, will undergo routine ROP assessment.

Inclusion Criteria[7]:

- Gestational age at birth <34-35 weeks.
- Birth weight <1700g
- Oxygen exposure >30 days.
- Other factors that can increase the risk of ROP and where screening should be considered are premature babies >37weeks or >1700g but with
  1. Respiratory distress syndrome
  2. Sepsis
  3. Sickly survivors
  4. Pneumonitis
  5. Multiple blood transfusions
  6. Multiple births (Twins/Triplets)
  7. Apneic episodes
  8. Intraventricular hemorrhage

Exclusion Criteria

1. Congenital anomalies of the eye
2. Chorioretinitis
3. Born after 36 weeks (excluding the above causes)
4. Birth weight >1700gm.(excluding the above causes)

Methodology

Written Informed consent was taken.

According to inclusion and exclusion criteria patients were chosen.

Approval from institutional ethics committee was taken. (IEC-38/2020-21)

Relevant detailed history of mother as well as baby was taken.

All infants were assessed by the same ophthalmologists.

Time of the Screening

Infants whose gestational age was greater than 28 weeks had their initial screening performed within 4 weeks (30 days) after delivery, or two to three weeks later if their birth weight was less than 1200g and gestational age less than 28 weeks.

Examination

- In the NICU, screening was conducted using a radiant warmer under the supervision of a neonatologist. In the OPD, stable and discharged infants had been evaluated. Before the examination, the assessment process was explained to the parents or guardians, and with their consent, the newborns were evaluated. The mother was instructed that the infant should be fed an hour prior to the assessment. Babies who needed to be in

an incubator were assessed there. 0.5% tropicamide plus 2.5% phenylephrine eye drops were used to dilate pupils 2-3 times, about 10-15 minutes apart each time, or until the desired level of dilatation was reached. Because overdosing involves the danger of tachycardia and hyperthermia, care was made to wipe off any excessive droplets to prevent systemic absorption via the cheek skin.

- Topical anaesthesia 2% paracaine drop was administered. A wire speculum for infant was used to keep their eyes apart. The globe was stabilized by mild indentation using a paediatric scleral depressor.
- A general anterior segment examination had been performed to check for lens/media clarity, Pupillary dilation, and Tunica Vasculosa Lentis.
- Posterior Segment Evaluation: Fundus examination using indirect ophthalmoscopy and a +20D condensing lens.
- The parents and neonatologist were both informed of the next follow-up date and given advice on it.
- In case of any apnoea or bradycardia during the assessment, resuscitation techniques were kept ready.
- The eye examination was terminated based on postmenstrual age or the retinal test findings when:

  1. There was proof of complete retinal vascularization, which usually takes 40 to 45 weeks to complete.
  2. ROP was regressed, as seen.

The newborns were checked for at least one to two weeks until they were 38 to 40 weeks old of postmenstrual age.

All of the infants who had Stage III ROP, A ROP, or Plus disease received laser photocoagulation treatment. The treatment took place in the NICU, which had monitoring and resuscitation equipment accessible.

Analysis of Statistics

For data collection Microsoft Excel was used. P value which was <0.05 considered as statistically significant.

Result

96 babies were screened during the study period of two years from October 2020 to December 2022.

96 babies which was fit into the inclusion and exclusion criteria were screened.63 (65.6%) out of 96 were male and 33(34.4%) out of 96 were female. In our study male predominance was observed which is shown in fig1 below.

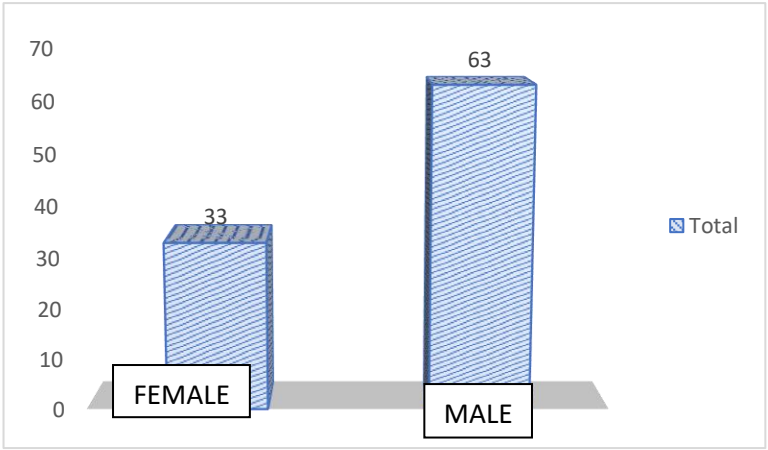


Figure 1. Showing Gender Distribution

Demographic History of the Mother:

Out of 96 babies 63(65.6%) babies were born at our hospital and 33(34.4%) were born outside other than our hospital. 49/96 (51.04%) babies were delivered vaginally while 47/96 (48.96%) were delivered by caesarean section. 25/96(26.04%) mothers had history of PIH. 2/96(2.08%) mothers had a history of gestational diabetes mellitus. 21/96 (21.87%) babies were of multiple gestations.

Demographic History of the Baby:

The average of birth weight was 1587±356.99 grams (range 965-3050 gm) and the average gestational age was 32.84 weeks (range 28-40 weeks) in our study. 24 out of 96 babies had ROP in our study. Thus, incidence of ROP was found to be 25% in the present study as shown in fig2 below.

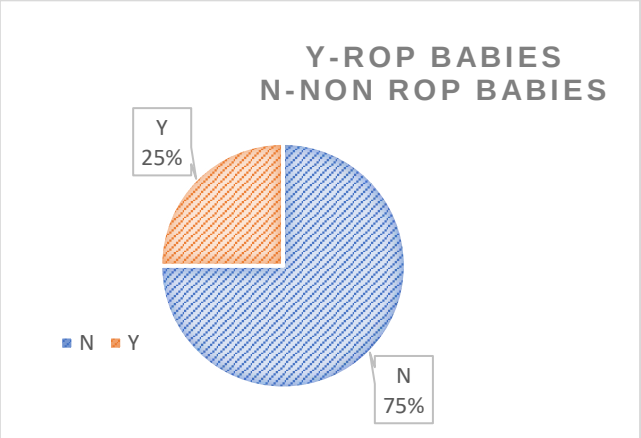


Figure 2: Incidence of ROP

ROP Data:

Examination initially was done between 3 and 7 weeks with an average of 4 weeks. Late referral of the infant from outside or late admission to our NICU and failure to screen externally might both have contribute to late screening. Total ROP positive male were16/24(66.66%) and female were 8/24(33.33%) (p value- 0.9012 which is statistically not significant) which is shown in fig3 below.

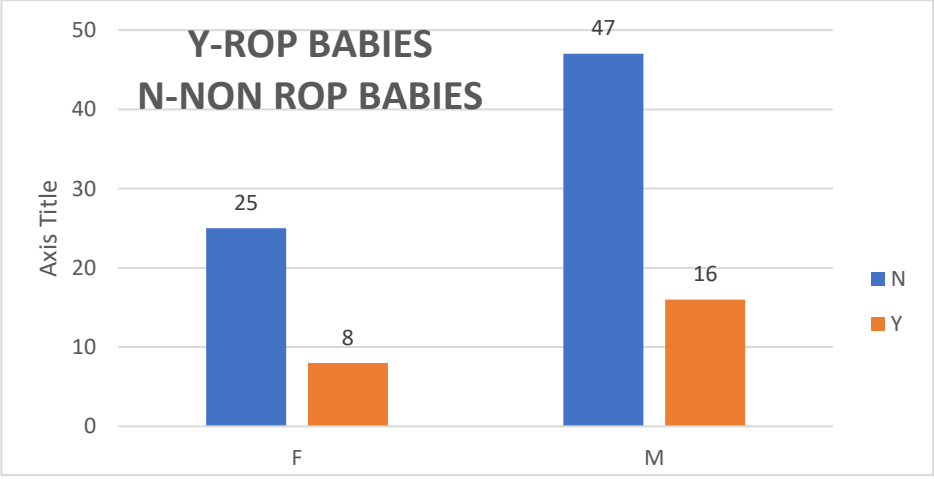
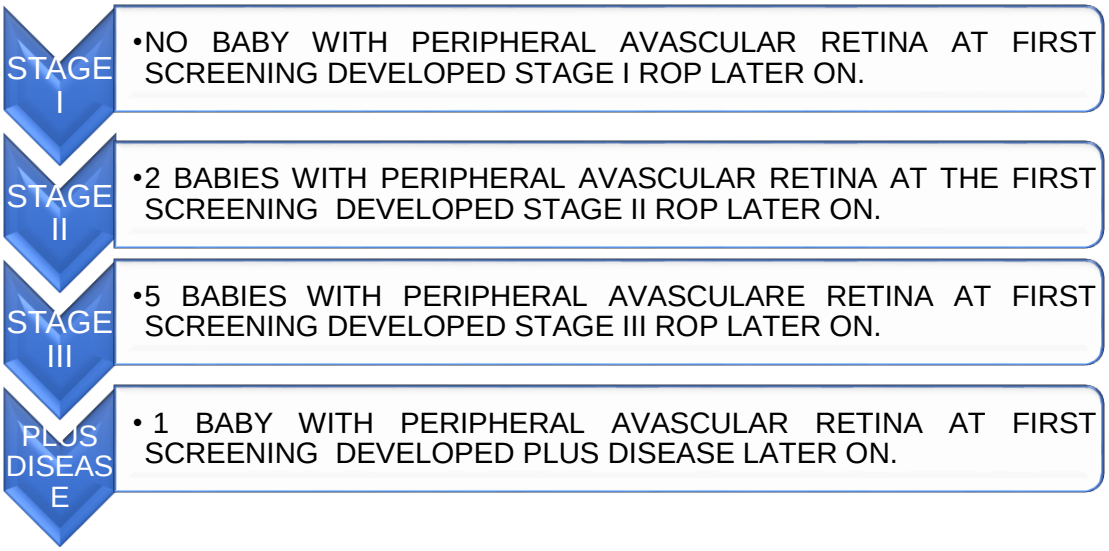


Figure 3. Gender Wise Distribution of ROP

Detection of First ROP:

16/24(66.66%) babies was found to have ROP on first screening and 1 of 16 had A-ROP which was lasered on same day. In 8/24(33.33%) babies had peripheral avascular retina which later developed ROP and 1 of 8 babies later developed PLUS disease.

Table 1: Showing Progression of ROP after 1st Assessment



The average birth weight of ROP at first detection was 1654.21 grams and average post conceptional age was 34.37 weeks which is shown in table2 below.

Table 2: Average Birth Weight and Post Coceptional age according to the Treated and Non-Treated ROP

	All ROP	Treated ROP	Non-Treated ROP
Average Birth Weight At First Detection (In Grams)	1654.21	1372.53	1560.45
Average Post Coceptional Age At First Detection (In Weeks)	34.37	33.38	35.54

Table 3 Distribution of Treated ROP and Non-Treated ROP According to the Birth Weight and Gestational Age at Birth

	ROP Treated N=13	ROP Non-Treated And Non Rop N=83	P values	Significance
Birth Weight In Grams				
≤1250	6	9	0.001	**Significant**
>1250	7	74		
Gestational Age In Weeks				
≤32 Weeks	9	28	0.014	**Significant**
>32 Weeks	4	55		

ROP Babies Requiring Treatment Data Analysis:

Out of 24 babies who developed ROP, 13 babies (26 eyes) had severe ROP in both eyes which was lasered. Average birth weight and gestational age of these babies were 1411.92 grams (range 1000-1900) and 30.84 weeks (range 28-34 weeks) respectively.

9/13(69.23%) babies i.e.(18/26 eyes) of these lasered ROP babies had gestational age ≤32 weeks and 4/13(30.76%) babies i.e.(8/26 eyes) had gestational age >32 weeks as shown in table 4.

8/13(61.54%) babies i.e.(16/26 eyes) of these lasered ROP babies had birth weight ≤1500 grams and 5/13(38.46%) babies i.e.(10/26 eyes) birth weight >1500 grams as shown in table 5.

The severity of ROP was more as the gestational age at birth and birth weight decreased was observed in our study. The maximum incidence of treated ROP was in gestational age ≤ 28 weeks (40%) and in birth weight ≤ 1250 (40%) which is shown in Table 4 and 5 respectively.

Table 4 Infants Requiring Treatment (Laser Therapy) according to Gesational Age

Gestational Age	Total Babies (N=96)	Total Eyes (N=192)	Lasered Babies (N=13)	Lasered Eyes (N=26)
≤28	10	20	4(40%)	8
29-30	9	18	3(33.33%)	6
31-32	18	36	2(11.11%)	4
33-34	43	86	4(9.30%)	8
35-36	9	18	0	0
37-38	3	6	0	0
39-40	4	8	0	0
>40	0	0	0	0

Table 5 Infants Requiring Treatment (Laser Therapy) according to Birth Weight

Birth Weight	Total Babies (N=96)	Total Eyes(N=192)	Lasered Babies (N=13)	Lasered Eyes (N=26)
≤1000	3	6	1(33.33%)	2
1001-1250	12	24	5(41.66%)	10
1251-1500	29	58	2(6.89%)	4
1501-1750	32	64	4(12.5%)	8
1751-2000	12	24	1(8.33%)	2
>2000	8	16	0	0

ROP Data According to the Stages

6 out of 24 (25%) i.e.12 eyes had Stage I ROP, 5 out of 24 babies i.e. 10 eyes had Stage II ROP, while 12(45.83%) babies i.e. 24 eyes had stage III ROP. 1 baby (2 eyes) had Aggressive ROP i.e. (4.16%) and 1 baby (2 eyes) had Plus disease (4.16%). No stage IV or V ROP as shown in Fig4.

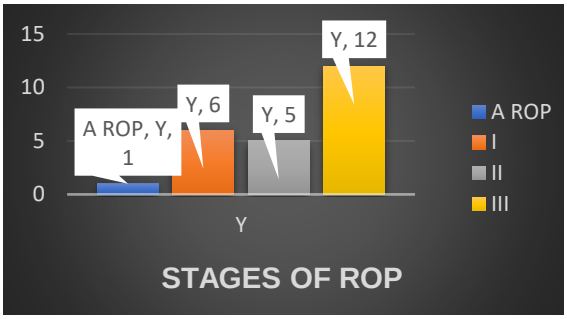


Figure 4: Stages of ROP

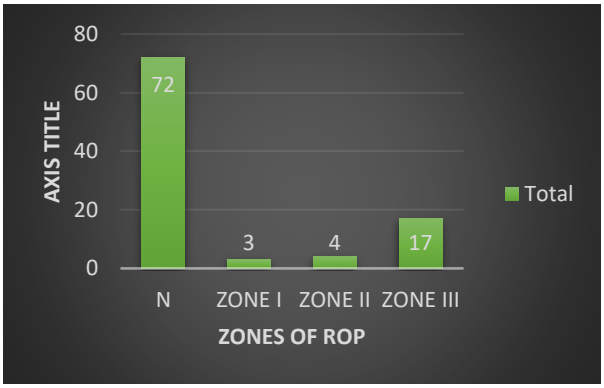
The mean birth weight in grams and mean gestational age in weeks according to the stages of ROP shown in the table6 below.

Table 6. Average Birth Weight and Gestational Age according to Stages

	Stage I	Stage II	Stage III, Plus Disease and A-ROP
Mean Birth Weight (Grams)	1513.33 ± 207.04	1672 ± 248.33	1395 ± 274.77
Mean Gestational Age (Weeks)	31 ± 2.56	33.6 ± 3.36	31 ± 2.46

ROP Data according to the Zones:

3/24(13.5%) babies had ROP in ZONE I, 4/24 (16.66%) babies had ROP in ZONE II, 17/24(70.83%) babies had ROP in ZONE III. In our study we found that maximum cases had ROP in zone III.



Risk Factors for ROP

Multiple neonatal risk factors which were studied in the present study and found to be significant using CHI-square test were Exposure To oxygen, Number of Days on O_2, Ventilation, Number of Days on Ventilation, Respiratory Distress Syndrome (RDS), Sepsis, Blood Transfusion, Apnoeic Episodes indicating an increased association with ROP.

In this study 22/24(91.66%) babies had exposure to the oxygen, 15/24(62.5%) were ventilated.17/24(70.83%) had culture proven sepsis,18/24(75%) had respiratory distress syndrome,13/24(54.16%) had apnoeic episodes and in 15 out of 24 i.e. (62.5%) multiple blood transfusion had been done. We also noticed one important risk factor in our study that was average number of days of O_2 exposure is more in ROP babies i.e. 30.45 days in comparison with NON-ROP babies which was on O_2 i.e.2.66 days which is shown in Table7 below.

Table 7. Data of Neonatal Risk Factors

Neonatal Risk Factors	ROP Babies N=24	Non-ROP Babies N=72	P Value	Significance
O_2 Exposure	22	27	<0.00001	**Significant**
Average No of days of O_2 Exposure	30.45	2.66	<0.00001	**Significant**
Ventilation	15	10	<0.00001	**Significant**
Average No of days on Mechanical Ventilation	6.833	0.708	0.0027	**Significant**
Multiple Births	6	15	0.6689	Non-Significant
RDS	18	23	0.00022	**Significant**
Sepsis	17	20	0.000175	**Significant**
Phototherapy	3	15	0.365	Non-Significant
Sickly Survivors	4	11	0.871	Non-Significant
Pneumonitis	6	18	1	Non-Significant
IVH	1	2	0.734	Non-Significant
Apnoeic Episodes	13	3	<0.00001	**Significant**
Blood Transfusion	15	26	0.0236	**Significant**

Table 8 is showing maternal risk factors which was not found to be significant in our study.

Table 8. Data of Maternal Risk Factors

	Mother of Rop Babies N=24	Mother of Non-Rop Babies N=72	P Value	Significance
Place Of Delivery 1.Hospital Delivery 2.Outside Delivery	 17 7	 46 26	0.5350	**Non- Significant**
Type Of Delivery 1.Vaginal 2.C-Sect	 15 9	 34 38	0.1947	**Non- Significant**
Gravida 1.Primigravida 2.Multigravida	 15 9	 39 33	0.7626	**Non- Significant**
Pih 1.Present 2.Absent	 8 16	 17 55	0.3473	**Non- Significant**
Gdm 1.Present 2.Absent	 1 23	 1 71	0.4093	**Non- Significant**

Discussion

ROP has become more common as a result of rising prematurity rates and smaller newborns having higher survival rates. In the current study, 96 infants were thoroughly evaluated

Association of Average Birth Weight and Gestational Age with ROP:

In our research, NONROP babies on average weighed 1618.79±379.6 g. (range 965-3050g). The average birth weight of ROP infants was 1491.45g. The average gestation period for NON-ROP infants was 33.31±2.43 weeks and the average gestational age of ROP infants was 31.41±2.82 weeks.

According to research by Mahuya Pal Chattopadhyay et al[8] the mean (SD) birth weight and gestational age of newborns with and without

ROP were 1410 ±350 g and 31.8 ±2.1 weeks, and 1820 ±440 g and 32.9 ±2.1 weeks, respectively.

Progression of ROP after First Detection

In the first screening, 16/24 (66.66%) newborns developed ROP. 8/24 (33.33%) of the newborns had avascular peripheral retina, which later developed ROP. 1/8 babies later developed PLUS disease. The average birth weight of all ROP infants at the time of the first diagnosis was 1654.21g and the average post-conceptional age at initial detection for all ROP was 34.37 weeks.

According to Shrutakirti Gosh et al[9] out of 70 patients, 17 (24.3%) had an immature retina at the time of the initial visit but later developed ROP. The remaining 53 individuals (75.71%) already had ROP at the initial visit.

According to A R Feilder et al[10] 86% of newborns who had retinopathy between 32.5 and 38.5 weeks of age showed the first indications of retinopathy of prematurity.

Distribution of ROP Stagewise:

The mean birth weight in the present study was decreased as the stage of ROP goes on increasing which was consistent with the studies done by Rohit Charan, M. R. Dogra[11].

Distribution of ROP Zonewise:

In current study, 3/24 (13.5%), 4/24 (16.66%), and 17/24 (70.83%) of the newborns had ROP in ZONE I, ZONE II, and ZONE III, respectively. According to Jasmina Alajbegovic-Halimic et al[12] study and **CRYSTAL Le et al[13]** in their investigation, discovered that patients with ROP were more frequently detected in ZONE III. These studies had similarity with our study.

ROP and Risk Factors Association:

Maternal Risk Factors:

In this study, we looked into maternal characteristics like gestational DM, PIH, gravida, place of delivery, and type of delivery. None of these factors were significant, according to our research.

Neonatal Risk Factors

The Univariate analysis of oxygen exposure, the average number of days spent in oxygen exposure, ventilation, the average number of days spent on mechanical ventilation, RDS, sepsis, apnoeic episodes, and blood transfusion were shown to be significant when the Chi Square test of significance was used.

Additionally, for all patients with severe ROP receiving therapy, blood transfusion, RDS, apnoea, and 02 exposure, mechanical ventilation as well as the number of days spent on mechanical ventilation and 02 were statistically significant risk factors.

We found this is similar with the studies done by Sudha et al[14] , Krishna A. Rao et al[15], Anjali Parekh et al[16], Gaber R et al.[17]

Conclusion

To ensure that no infants with ROP are missed and to lessen the burden of blindness brought on by ROP, we need a stricter guideline rather than one that are optional. This will help in early assessment and detection of preventable ROP complications which land up into blindness and restrict the progression of disease as early as possible.

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Conflicts of interest: None

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